“THE ROLE OF IMMUNOCHROMATOGRAPHIC ANTIGEN DETECTION ASSAY IN THE EARLY DIAGNOSIS OF MALARIA"

Dissertation submitted to

THE TAMIL NADU DR.M.G.R.MEDICAL UNIVERSITY

In partial fulfillment of the regulations for the award of degree of

M.D DEGREE (PEDIATRICS) BRANCH VII

DEPARTMENT OF PEDIATRICS

GOVT STANLEY MEDICAL COLLEGE

CHENNAI – 600 001

APRIL 2015

DECLARATION

I, **Dr.R.Anand** solemnly declare that the dissertation titled **"THE ROLE OF IMMUNOCHROMATOGRAPHIC ANTIGEN DETECTION TEST IN THE EARLY DIAGNOSIS OF MALARIA"** was done by me at **Stanley Medical College during 2013- 2015** under the guidance and supervision of my chief **Dr.SUJATHA SRIDHARAN M.D, D.C.H.**

The dissertation is submitted to **The Tamilnadu Dr.M.G.R. Medical University** towards the partial fulfilment of the rules and regulations for the **M.D. Degree Examination - BRANCH VII –in Paediatrics**.

Signature of the candidate

Place : Chennai **Dr.R.ANAND**

Date:

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation titled **"THE ROLE OF IMMUNOCHROMATOGRAPHIC ANTIGEN DETECTION TEST IN THE EARLY DIAGNOSIS OF MALARIA"** is a bonafide research work done under my guidance by **Dr.R.Anand,** Postgraduate student, Department of paediatrics, Govt. Stanley Medical College, The Tamilnadu Dr.M.G.R Medical University, Chennai , in partial fulfilment of the requirement of the award for the degree of **M.D PAEDIATRICS - BRANCH VII.**

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CERTIFICATE BY THE INSTITUTION

This is to certify that the dissertation titled **"The role of immunochromatographic antigen detection test in the early diagnosis of malaria"** is submitted by **Dr.R.Anand** to **The Tamilnadu Dr.M.G.R Medical University, Chennai- 01** in partial fulfilment of the requirement of the award for the degree of **M.D BRANCH VII (PAEDIATRICS)** and is a bonafide work done by him under our direct supervision and guidance, during the academic year 2013 -2014.

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LIST OF ABBREVATIONS

pLDH	-	Plasmodium Lactate Dehydrogenase
PBS	-	Peripheral blood smear
QBC	-	Quantitative buffy coat
Pl.	-	Plasmodium
NMCP	-	National malaria control programme
G6PD	-	Glucose 6 phosphate dehydrogenase
RBC	-	Red blood cell
DIC	-	Disseminated intravascular coagulation
Hb	-	Hemoglobin
PCV	-	Packed cell volume
UTI	-	Urinary tract infection
LBW	-	Low birth weight
HIV	-	Human immunodeficiency virus
HbF	-	Fetal hemoglobin
ARF	-	Acute renal failure
WBC	-	White blood cell
FFP	-	Fresh frozen plasma
i.v.	-	Intravenous
EBV	-	Ebstein Barr Virus
AO	-	Acridine orange
HRP-2	-	Histidine rich protein -2
RDT	-	Rapid diagnostic test
PPV	-	Positive predictive value
NPV	-	Negative predictive value
HMW	-	High Molecular weight
ARDS	-	Acute Respiratory Distress Syndrome

ABSTRACT

Background and objectives:

This study is conducted on the OP/IP patients visiting the Institute of social paediatrics, Stanley medical college, Chennai 01. It identifies the efficiency of immune chromatographic method to detect malaria as compared to the peripheral blood smear examination, which is considered as the gold standard.

Method:

The children with clinical features of malaria are subjected to this test. The test detects the histidine rich protein 2 and pan lactate dehydrogenase of the malarial parasite. HRP 2 is specific for Plasmodium falciparum and P LDH is produced by all species of malaria. The test results are compared with the results obtained by peripheral smear.

Results:

The test kits showed 23.1% cases positive by the card test, the peripheral smear should 20% positive. The card was 91.3% sensitive,

peripheral blood smear 100%, the card was 96.3% specific and the PBS 98.7%. The two tests showed comparable results.

Conclusion:

The card test showed similar sensitivity and specificity pattern as the peripheral blood smear. Being easier to handle this card will be of great use in resource constrained settings in rural India

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ம□ல□ய□ க□ய்ச்சல் அறி□றிகள் உள்ள □ழந்□தக□ க்□ எ□ தல் கண்□பி□க்கக் □ □ய இரத்த □ச□த□ன □□ற பற்றி ஆர□ய்தல்

ஆர□ய்ச்சி ரி□லயம் : □ழந்□தகள் ச□க நல ம□த்□வப்பி□□ அர□ ஸ்ட□ன்- ம□த்□வமன□, □சன்□ன - 600 001.

பங்□ □பதிம் □ந□ய□கி □ன் □பயர் : வய□

பங்□ □பதிம் □ந□ய□கி □ன் எண் : ப□ னம்: ஆண் □ □பண் □

□ந□ய□கி □ன் நி ல□சம் :

□ந□ய□கி இத□ன (✓) □றிக்க□ம் :

□ம□ல □றிப்பிட்□ள்ள ம□த்□வ ஆய்நி ன் நி வரங்கள் எனக்□ நி ளக்கப்பட்ட□. என்□ □டய சந்□தகங்க□ள □கட்க□ம், அதற்க□ன த□ந்த நி ளக்கங்க□ள □பற□ம் வ□ய்ப்பக கப்பட்ட□. □

நட□ன் என் □ழந்□த□ய தன்□ ச்□சய□க்த□ன் பங்□கற்க அ□ ம□க்□□றன். எந்த க□ரணத்□ன□□ல□ எந்த கட்டத்□□ம் எந்த சட்ட சிக்க□க்□ம் உட்பட□மல் என் □ழந்□த□ய இவ்வ□ய்நி ல் இ□ந்□ நி ல□க்□ □க□ள்ளல□ம் என்தி அறிந்□ □க□ண்□டன். □

இந்த ஆய்□ சம்பந்தம□க□ம் □ம□ம் இ□த ச□ர்ந்த ஆய்□ □மற்□க□ள்□ ம் □ப□□ம் இந்த ஆய்நி ல் பங்□□பதிம் ம□த்□வர் என் □ழந்□த□ன் ம□த்□வ அறிக்□கக□ள ப□ர்ப்பதற்□ என் அ□ ம□ □த□வ□ல்□ல என அறிந்□ □க□ள்□□றன். என் □ழந்□த□ய ஆய்நி ல் இ□ந்□ நி ல□க் □க□ண்ட□□ம் இ□ □ப□□ந்□ம் என அறி□□றன். □

இந்த ஆய்நி ன் □லம் □□டக்□ம் தகவல்க□ளா ம், ப□□ச□த□ன □□□க□ளா ம் மற்தி ம் சி□ச்□ச □த□ர்ப□ன தகவல்க□ளா ம் ம□த்□வர் □மற்□க□ள்□ ம் ஆய்நி ல் பயன்ப□த்□க் □க□ள்ள□ம் அ□த பிர□□க்க□ம் என் □□ மன□டன் சம்ம□க்□□றன். □

இந்த ஆய்நி ல் பங்□ □க□ள்ள ஒப்□க் □க□ள்□□றன். என் □ழந்□தக்□ □க□□க்கப்பட்ட அறி□□ரகி ன்ப□ நடத்□ □க□ள்வ□டன் இந்த ஆய்□வ □மற்□க□ள்□ ம் ம□த்□வ அ□ க்□ உண்□மா டன் இ□ப்□பன் என்தி ம் உதி□ அகி க்□□றன். என் □ழந்□த□ன் உடல் நலம் ப□□க்கப்பட்ட□□ல□ அல்ல□ எ□ர்ப□ர்த்த வழக்கத்□ற்□ ம□ற்ன □ந□ய்க்□றி □தன்பட்ட□□ல□ உட□ன அத□ன ம□த்□வ அ□ க்□ □த□நி ப்□பன் என உதி□ அகி க்□□றன்.

இந்த ஆய்நி ல் என் □ழந்□தக்□ இரத்தம், சிதி □ர், எக்ஸ்□ர், ஸ்□கன் உட்பட அ□னத்□ ப□□ச□த□னக□ளா ம் □சய்□ □க□ள்ள ந□ன் □□ மன□டன் சம்ம□க்□□றன்.

பங்□கற்பவ□ன் □க□ய□ப்பம் ..... இடம் ..... □த□ .....

கட்□ட நி ரல் (இந்த ப□வம் ப□த்□ க□ட்டப்பட்□ □□ந்□ □க□ர□க அகி க்□□றன்)

பங்□கற்பவ□ன் □பயர் மற்தி ம் நி ல□சம் .....

ஆய்வ□ள□ன் □க□ய□ப்பம் ..... இடம் .....□த□ .....

ஆய்வ□ள□ன் □பயர் .....

தகவல் ப□வம்

ம□ல□ய□ க□ய்ச்சல் அறி□றிகள் உள்ள □ழந்□தக□ க்□ எ□ தல் கண்□பி□க்கக் □ □ய இரத்த □ச□த□ன □□ற பற்றி ஆர□ய்தல்

ஆர□ய்ச்சி□ன் □ந□க்க□ம், பயன்க□ ம் :

ம□ல□ய□ க□ய்ச்சல் உள்ள அறி□றிக□ள□□ வரக்□ □ய □ழந்□தக□ க்□, வழக்கம□க ப□□ச□த□ன □சய்யக்□ □ய இரத்தப்ப□□ச□த□னக□ள□□ □□ய □□ற□ல் அ□□வகம□க கண்□பி□க்கக்□ □ய இரத்தப் ப□□ச□த□ன□ய □சர்த்□ □சய்□, ப□□ச□த□ன□ன் ப- ன□ம□ய கண்டறிதல் அதன் □லம் நி ய□□□ய ச□ உப□க நி □ரநி ல் கண்□பி□த்த

ஆய்□ ந□ட□□றகள் :

சி□ச்□ச அகி ப்பதற்□ ஏற்ப□□ □சய்தல் இவ்வ□ர□ய்ச்சி□ன் □ந□க்கம□□ம். உள்□ந□ய□கி களக அல்ல□ □வகி □ந□ய□கி ய□க உள்ள ம□ல□ய கய்ச்சல் அறி□றிகள் உள்ள □ழந்□தகள் இந்த ஆர□ய்ச்சி□ல் □சர்த்□க் □க□ள்ளப்ப□வ□ர்கள்.

அந்தரங்க தன்□ம :

உங்கள் □ழந்□த□ன் ம□த்□வ ப□□வ□கள் □க□ம் அந்தரங்கம□க □வத்□க் □க□ள்ளப்ப□ம் மற்தி ம் பிற ம□த்□வர்கள் / நி ஞ்ஞ□□ கள் / இந்த ஆய்நி ன் த□ க்□கய□ளர்கள் அல்ல□ ஆர□ய்ச்சி ஆதரவ□ளர்ககி ன் பிர□ ரி□கள் ஆ□□ய□□டம் அ□வ □வகி ப்ப□த்தப்ப□ம். இந்த ஆய்நி ன் □□□கள் அறிநி யல் பத்□□க்□ககி ல் ப□□□க்கப்படலம். ஆனல் □பய□ர □வகி □□வதன் □லம் □ந□ய□கி □ன் அ□டய□ளம் க□ட்டப்பட ம□ட்ட□ர்கள்.

ஆய்□ ல் உங்கள் பங்□கற்□ மற்□ ம் உங்கள் உ□□மகள் :

இந்த ஆய்நி ல் உங்கள் □ழந்□தகி ன் பங்□கற்□ □□வ□ம் உங்க□ □டய நி □ப்பத்□த ச□ர்ந்த□. இ□ல் □ங்கள் பங்□கற்க□வ□, மதி க்க□வ□, ப□□□ல் □வகி □ய□ட□வ□ அல்ல□ □றிப்பிட்ட □கள்நி க□ க்□ பலகி க்க மதி க்க□வ□ உங்க□ க்□ □□ உ□□ம உண்□ எப்ப□ இ□ந்த□□ம் உங்கள் □ழந்□த□ன் உடல் ரி□லக்□கற்ப உங்கள் □ழந்□தக்□ □ப□□த்தம□ன சி□ச்□ச அகி க்கப்ப□ம் த□ங்கள் இ□ □றித்□ □வதி நி பரங்கள் □த□ந்□ □க□ள்ள நி □ம்பினல் எங்ககி டம் □கட்□த் □த□ந்□ □க□ள்ளலம்.

□ம□ம் நி பரங்கள் அறிய □ழ்க்கண்ட நப□ர அ□ க□ம் :
ம□.இர□ஆனந்த்
பட்ட□மற்ப□ப்□ ம□ணவர்
□ழந்□தகள் நல ம□த்□வம்
அர□ ஸ்ட□ன்- ம□த்□வ கல்□ □, □சன்□ன
□த□□லப்□பசி எண்.9003835452

INTRODUCTION

Malaria is an infection caused by parasite of Plasmodium species. It is prevalent over hundred countries across the globe. More than 1.6 billion people are exposed or at risk of infection throughout the world.

The prevalence of this infection is maximum in Africa, Asia, South America. These areas are in the tropical zones hence an ideal place for breeding of mosquitoes. The temperature, humidity, rainfall all favours the multiplication of mosquitoes and simultaneously the species causing malaria.

Since India falls in the tropical zones, our country also forms the endemic home of malaria. Myanmar, Bangladesh, India, Indonesia[3] account for large number of cases in Southeast Asia.

The dominant species in India is the Plasmodium vivax, next is Plasmodium falciparum[4]. The latter is the most fatal of the four species infecting man. The mortality is mainly encountered in young children and pregnant women who are vulnerable to the complications of malaria, due to the lowering of acquired immunity.

In the setting of low prevalence and low resistance zones, erratic use of antimalarials[6] causes the disease symptoms but there is no parasite clearance.

The parasite gains resistance to drugs and symptoms recur. The physician thinks it is a fresh infection and treats. The resistant parasite is now transferred to the other patients. This cycle ensures conversion of zone of high incidence and mortality.

Hence, cure is defined as complete elimination of the parasite from the host. Treating non-malarial cases with antimalarial drugs or irregular intake and premature stoppage of drugs before parasite clears in the peripheral blood contributes to drug resistance and aggravation of the problem and spread. Malarial card test is accurate, reliable and does not require skilled personal or equipment[7]. Hence it forms an excellent bridge for the diagnosis of malaria in resource constrained rural setting.

REVIEW OF LITERATURE

The tropical countries cater the most number of cases of malaria, and it forms the most important infections causing mortality in this locality. Among the four species causing human infection Plasmodium falciparum is the leader in the race in terms of morbidity and mortality.

The HRP 2/PLDH test detects antigens in the blood of malaria patients with a minimum of 5 µL of blood. The test is simple and effective, able to detect the parasite in a minimum period of 10 to 15 minutes. India is a country which caters two species of malaria Plasmodium falciparum and Plasmodium vivax.

Palmer et al studied the number of cases positive by rapid diagnostic test and the peripheral blood smear and found 45% and 48% respectively. The sensitivity of rapid diagnostic test for Plasmodium falciparum was 88% and specificity 99%, as far as vivax is concerned sensitivity 94% specificity hundred percent

Jelinek et al found peripheral blood smear positive by 29.8% and HRP2/PLDH by 24.2%. The sensitivity of Jelinek et al 88.5% 99.4% for Plasmodium falciparum under for vivax 61.5% and hundred percent. The

positive predictive value and negative predictive value for vivax and falciparum was around 98% – 100%.

Chayani N et al showed positivity of peripheral blood smear and HRP2/PLDH to be 52.5%, 50.8%. This study identified that the rapid diagnostic test have a sensitivity and specificity of 92%-100% for Plasmodium vivax and Plasmodium falciparum. Similar results were observed in other studies done by Jamshed Iqbal et al, in the year 2003 and 2002.

The positive predictive value, the negative predictive value, the sensitivity, the specificity are determined the diagnostic power of the test. The above studies demonstrate that the rapid diagnostic test which detects antigen in the blood of patients with malaria are highly sensitive, specific, having a positive predictive value of 88% – 98% in case of Plasmodium falciparum. The about test done for Plasmodium vivax was around hundred percent positive predictive value to 99% negative predictive value. All the above tests were compared with the gold standard in the diagnosis of malaria the peripheral blood smear.

HISTORY

The word "MALARIA" is derived from the word MAL meaning BAD, ARIA-meaning AIR, and the word meaning BAD AIR of the swamp[8]. This terminology for malaria was coined in the 17th century.

Fifth century BC: – Hippocrates used the words tertian, quartan, to describe the fever of malaria based upon its periodicity.

1600 :-the bark of cinchona was found to cure the disease in peru in South America next time.

1880 :-Charles identified the protozoa present in the blood sample of a patient with malaria.

1691 :-Erythrocytic phase of the parasite was accurately stained by Ramanosky[8].

1897 :-William McCullum documented that the malarial parasite had a sexual cycle.

1898 :-Ronald Ross identified malaria in the birds who were beaten by the mosquito[8]. The avian malaria was identified.

1948: Pre– erythrocytic stage present in the man was identified by Bray&shoff.

EPIDEMIOLOGY

There are 300 – 500 million cases affected by the disease per year. About 1 million death is encountered[1]. The most important reason for the death is the delay in the diagnosis, the delay in institution of therapy. Both the above factors can be drastically reduced if appropriate measures are undertaken appropriate times.

AGENT

The position of the malarial parasite in the taxonomical nomenclature is.

Kingdom – Animalia.

Phylum – protozoal.

Class – Sporozoa.

Order – Eucoccida.

Family – Plasmodia.

Genera – Plasmodium

Species – falciparum, vivax, ovale, malaria etc...

Of the several species of malarial parasite the two most important seen in India are

1) Plasmodium vivax – 70%

2) Plasmodium falciparum – 25%

Both the species account for about 95% of the infection due to malaria caused in India[10]. The other two plasmodia of human importance are:

1) Plasmodium ovale

2) Plasmodium malariae.

ROUTES OF TRANSMISSION:

1) The parasite lodge in the salivary gland of the female Anopheles mosquito, during the blood meal the parasite is injected into the human host. The mosquito then sucks the blood from the human body.

2) Injection of contaminated blood through blood transfusion, using the same needle in drug addicts form a rare source of malarial infection to man. This mode of transmission attains minimal importance.

FEMALE ANOPHELES MOSQUITO

The name Anopheles is derived from the Greek word ANO- meaning not, pheles – meaning profit. Put together the word meaning of Anopheles is 'useless '.

The Anopheles mosquito act as a vector of 1) malaria

2) filaria

3) some viruses.

The important behaviour of mosquitoes that make them effective vectors[11] of man are their anthrophilic nature, they feed on human or cattle blood for the development of the malarial eggs in the stomach of the female anopheles mosquito. This character of the mosquitoes make them effective vectors for the transmission of malaria.

The extrinsic incubation period of malarial parasite is about 10 to 21 days. Any malarial parasite which can survive a period less than this does not become an effective vector for malaria.

Genetically modified mosquito when the multiplication of malarial parasite inside the gut of the mosquito. The most the important vectors in India for transmission of malarial infection are,

1) Anopheles culicifacies – rural areas

2) Anopheles stephensi – urban areas.

Entomological inoculation rate or the number of bites sustained by individual per day determines the transmission rate[12]. This factor depends upon the mosquito density, temperature, population growth and migration, drug and parasite resistance, lastly the deterioration of health care services.

ENDEMIC: – EN (in); DEMOS (population)

A disease or condition regularly found among the particular people or certain area is known as an endemic disease.

EPI DEMIC: – EPI (upon); DEM OS (population)

Widespread occurrence of an infection or disease more than the expected occurrence at the time is known as epidemic.

TRANSMISSION OF MALARIA:

The transmission of malaria depends upon three variables, they can be the host – human being, the agent – the mosquito, the environment – the climatic conditions.

1) THE CLIMATE:

The temperature between 16 to 33°C provide the ideal environment for the transmission of malaria. The altitude[11] of greater than 2000 m does not favour malaria transmission.

Permanent shallow sunlit pools of water with the perimeter of greater than 10 m, with the absence of surface run-off, the base formed by Clay which can hold water forms an ideal place for breeding of the vectors of malaria.

The relative humidity present in the tropical countries is appropriate for the breeding of mosquitoes here. India being among the tropical countries forms and endemic home of malaria.

THE AGENT:

The Plasmodium as a complex life cycle in humans. This enables them to live and survive in different human cellular environment makes them resistant to elimination.

The malarial parasite escapes the host immune system by exhibiting antigenic diversity as well as several other immunomodulatory functions.

THE HUMAN FACTORS:

Human factors play an important role in the transmission of malaria in the regional as well as international arena, the factors favouring transmission of as follows:

1) human migration – spreads infection from one place to another, from one geographical area to another making it a worldwide disease.

2) social economic status – people living low social economic status are prone for malarial infection since the entomological inoculation rate for this group of population is highly. They lack effective shielding from mosquitoes due to lack of pukka houses, sanitation, nets etc.

3) immune status of the individual – persons living in endemic areas have high level of immunity protecting them from infection.

EPIDEMIOLOGICAL INDICES OF MALARIA

1. Pre-eradication era

a) spleen rate: – estimates the burden of malaria transmission in

b) parasite rate: – this is used along with spleen rate

c) parasite density index: – index of degree of parasitaemia.

d) infant parasite rate: – very sensitive for malaria transmission[10].

e) average spleen rate.

2. Eradication era

a) API – annual parasite index: – incidence indicator

Total number of confirmed cases in a year/population multiplied by thousand.

b) ABER – annual blood examination rate: index of operational efficiency.

ie = Total number of slides seen/population under surveillance multiplied by thousand.

THE MOSQUITO:

By mutual adaptation between Anopheles and the Culex mosquito, the Anopheles mosquito has now adapted to grow in polluted waters as Culex mosquitoes. Hence the limitation barrier in the cities as been bypassed favouring multiplication of Anopheles mosquito in the city's.

STABLE TRANSMISSION:

A continuous exposure to a fairly constant and high rate of malarial parasite in the tropical regions such as sub Saharan Africa results in development of partial immunity. The average entomological inoculation rate is greater than 10, hence people living in this area develop resistance at a younger age, this contributes to the stable transmission in this area.

UNSTABLE TRANSMISSION:

The areas with entomological inoculation rate of less than five the acquired immunity is not developed. The population remains vulnerable to the infection. All the age groups affected, the frequency and severity of malaria increases as the mosquito density and biting rate increases rapidly example Asia. India falls into this group of population where there is unstable transmission and the people are prone for the infection and its complications.

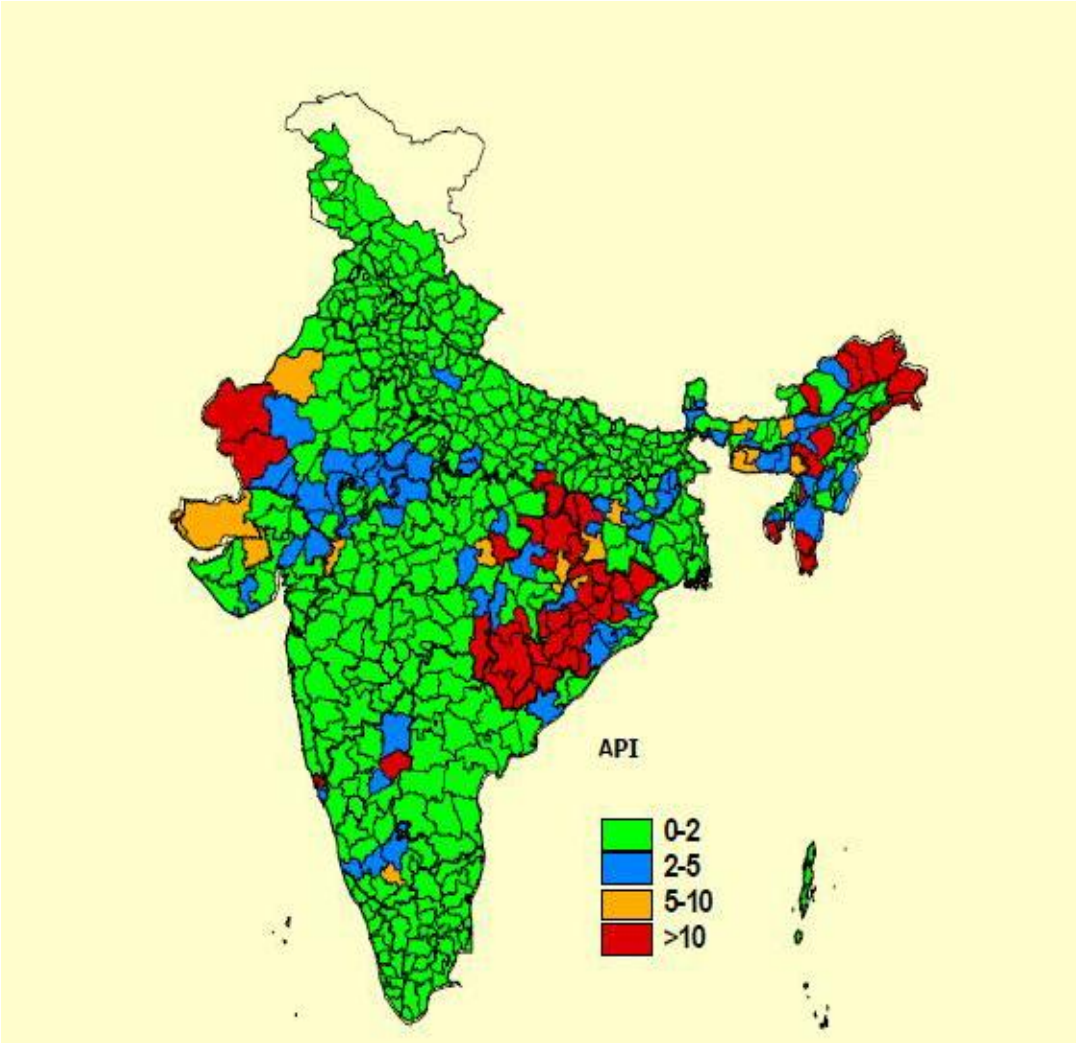


FIGURE 1 MALARIA ENDEMIC AREAS IN INDIA

HYPOENDEMIC--<10%.

MESOENDEMIC--10%-50%

HYPERENDEMIC--50%-75%

HOLOENDEMIC-->75%

GENETIC FACTORS :

In areas of stable transmission, where the entomological inauguration rate is greater than 10 per year the human body adapts genetically to this infection by forming resistance to it.

1) Duffy negativity of the RBC's protect against Plasmodium vivax. This has virtually led to the elimination of malarial parasite in the African countries[11].

2) Thalassaemia causes 50% reduction in malarial infection.[11]

3) homozygous haemoglobin C – 90% reduction.

4) haemoglobin E and ovalocytes carrier state protect Plasmodium falciparum and Plasmodium vivax.

5) sickle cell anaemia gives 90% protection.

6) G6PD gives 50% production against infection.

LIFE CYCLE:

In the life cycle of malarial parasite man forms the intermediate host since he harbours the asexual form of the parasite.

1) human host – asexual phase – intermediate host.

2) mosquito – sexual phase – definite host.

IN THE INTERMEDIATE HOST MAN:

In humans, the malarial parasite existing various forms forming a complex life cycle, this enables the parasite to live in different adverse environments in the body.

The bite of the female Anopheles mosquito inoculates the sporozoite into the bloodstream, within minutes the sporozoites reaches the liver parenchyma.

Amplification of the parasite occurs in two step process. The first phase forms the hepatic phase. Here the tissue scizhonts increase in number to about 10^2 to 10^ 14. The second step occurs on the RBC, this is called the area erythrocytic phase.

In the liver (schizont) undergo multiplication and at one stage burst out of the liver. They are released into the circulation and are called the merozoites.

The hepatic phase of malarial parasite, the patient remains asymptomatic. The reason for the lack of specific symptoms is that the schizonts are remaining intracellular. There not exposed to the host defences and they are not eliminated.

ERYTHROCYTIC SCHIZOGONY:

The tissues SCHIZONTS of the release from the liver cells are called MERROZOITES.

There are two types of phenomenon after rupture of liver PHASE parasites – one the Plasmodium falciparum/Plasmodium malaria – do not reinfect the cells. Second Plasmodium ovale/Plasmodium vivax persist in the liver as Hypnozoites.

Inside the RBC the parasite transfers into ring forms which enlarges into early trophozoites.

Staining with Romanowsky or Giemsa stain can be done and trophozoites and merozoites can be seen. The trophozoites multiply and released in circulation as erythrocytic schizont.

The trophozoites converted to late trophozoites by feeding on the haemoglobin present on the RBC. The haemoglobin is only partially metabolised leaving behind the malarial pigment called hemozoint pigment.

The late trophozoites give rise to early schizonts which on multiplication converted to late schizonts and released into the circulation. The cycle keeps repeating.

With each spike of fever the RBC's lysis occurs, erythrocytic schizonts are released and the cycle gets synchronised.

Table 1: Characteristics of Plasmodium species infecting humans

Characteristic feature	**Plasmodium falciparum**	**Plasmodium vivax**	**Plasmodium ovale**	**Plasmodium malariae**
Exo-erythrocytic phase (days)	5.5	8	9	15
Hepatic phase number of merozoites	30,000	10,000	15,000	15,000
Erythrocytic phase duration in hours	48	48	48	72
Red blood cell preference	Younger cells	Reticulocytes	Reticulocytes	Older cells

GAMETOGONY:

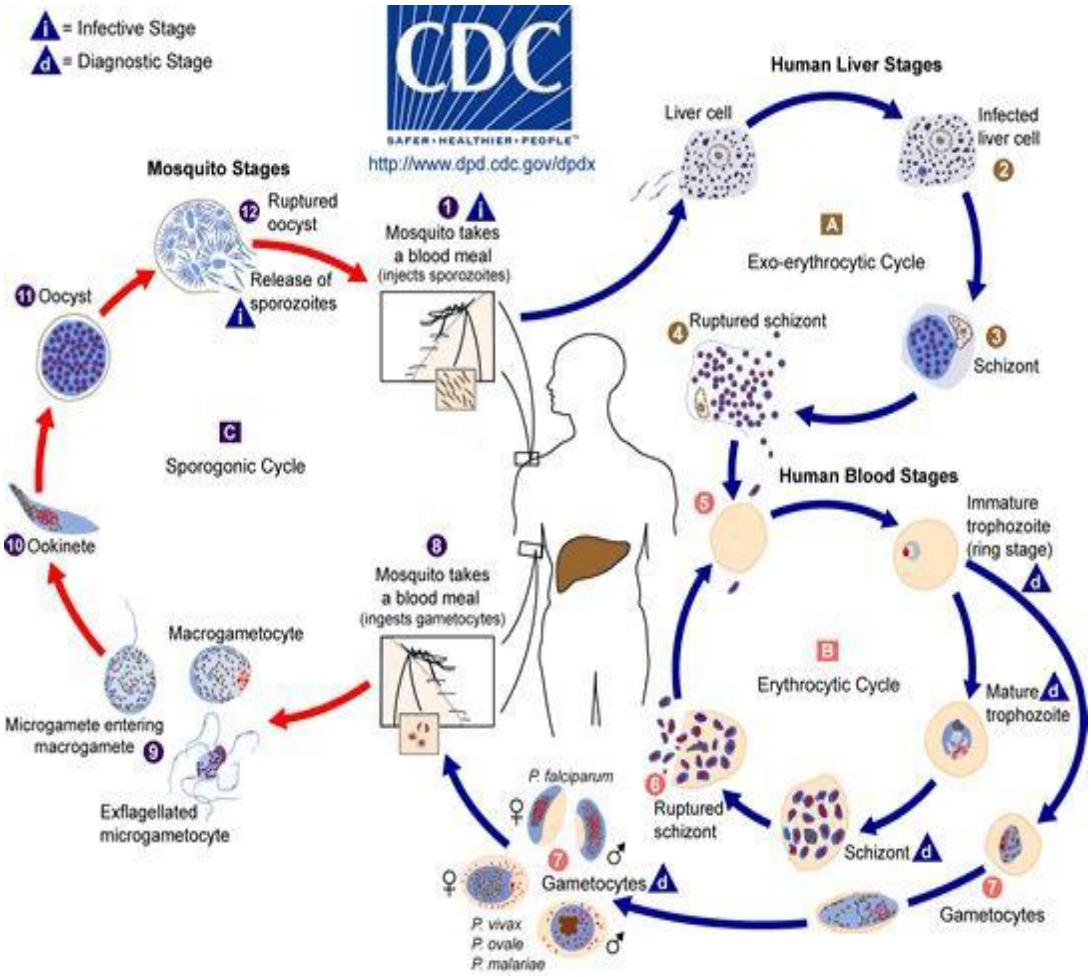
Over time, some of the merozoites develop into male, female gametocytes and enters into the mosquito during their blood meal, fuse in the stomach of the mosquito forming the zygote hence completing the malarial life cycle.

The male and female gametocytes entry into mosquito and reproduction by sexual means marks their sexual phase of the malarial life cycle. The host being the definitive host.

The minimum concentration of gametocytes required to infect the mosquito is 12/cubic millimetre of blood. Apart from forming the infective stage of the life cycle they do not produce any pathological effects in the host. The gametocytes if they do not fuse, that this they are not taken up by the mosquito then they wither of in a few days time.

The formation of the gametocytes occurs in the spleen in the bone marrow whereas in the peripheral blood only the mature forms of the parasite are seen, the premature forms are found in the spleen and bone marrow. This constitutes the carrier or reservoir of infection.

Fig 2: LIFE CYCE OF MALARIA



RELAPSE

When resource of malaria infection is an EXO-erythrocytic phase then it is called relapse.

Exo – erythrocytic source such as the liver is seen in Plasmodium vivax, Plasmodium ovale.

The merozoites in the liver after multiplication bursts open the hepatocytes and enters the blood. It has been considered the released merozoites are two sizes. The smaller ones runs into the blood, the larger ones remain in the liver. This reinfect the liver and forms the basis of the next relapse. The cells are called the hypnozoites.

HYPNOZOITE THEORY:

In certain species of malaria, that is Plasmodium ovale and Plasmodium vivax, this SCHIZONTES multiply in the liver to release two types of merozoites.

The smaller sized merozoites are released into the circulation and causes clinical manifestations.

The larger ones reinfect the liver cells and remained dominant in the cells. These are called the hypnozoite's and are responsible for relapse

RECRUDESENCE:

This is caused by survival of the parasite in the erythrocyte for long periods at low levels escaping the host defence mechanisms. This is seen in certain species of malaria such as Plasmodium falciparum.

There is total absence of parasite in the tissue phase, hence radical cure with primaquine is not required for this type of malaria. Hence the distinction between recrudescence and relapse becomes important to plan the further course of management.

The usual treatment given for malaria is to cure the disease, and cure the disease there is a need for early identification of the infection and also the type of infection.weeks, months, years later.

MALARIA AND HUMAN HOST:

The malarial parasite escapes the host defence mechanism by the following means,

1) Antigenic diversity, clonal antigenic variation: each Plasmodium has different antigens as well as the change in the antigenic structure during the course of infection.

2) Immune modulation: Hemozoin in the malarial cell decreases the maturation of antigen presenting cells such as the macrophages which ingest these have pigments present in the bloodstream or RBC. This results in immunosuppression and the aggravation of bacterial infections during the course of malarial infection.

On entry into the human immune system there is activation of non-specific immune response, humoral response such as non-specific polyclonal activation and the specific Ig.

Non-specific activation of immune system – there is non-specific polyclonal activation of the immune system who significance is not known. The natural killer cells produce interferon, in response to parasitised RBC leading to macrophage activation and causing the death of RBC.

Interleukin eight the pro-inflammatory cytokine aggravates the immune response to the malarial parasite.

(3) The development of cellular defence mechanism are impaired in protein energy malnutrition[11], HIV infection[12], antigenic diversity of the malarial parasite, lack of major histocompatibility complex on the surface of infected RBCs.

PREMUNITION:

It is the immunity in the host mediated by the presence of parasite itself and not as a result of previous infection. In areas such as sub-Saharan Africa[2] the entomological inoculation rate exceeds greater than 10 to about 70 per day. This results in high blood levels of parasitaemia and activation of host immune responses. The end result the individual remains partially immune to the infection. This is known as premunition.

PATHOPHYSIOLOGY:

Malarial infection in human beings resulting clinical manifestations which are a result of the following for pathological events,

1. fever
2. pallor due to anaemia
3. immuno pathological events
4. tissue anoxia.

All the acute events are caused by the blood stage malarial parasite and not by the intracellular located malarial parasite.

a) Anaemia – in infection with malaria anaemia results due to haemolysis during the febrile paroxysm, the parasitised RBCs also taken up by the spleen (splenic sequestration). The bone marrow undergoes suppression due to the inflammatory cytokines released by the blood stage malarial parasite when the RBC lysis during the febrile paroxysm.

b) Immuno pathological events – non-specific polyclonal activation of B lymphocytes occurs in malaria leading onto various immune complex mediated diseases. The TNF alpha released during the inflammation also causes deteriorating effects in the patient.

c) Tissue anoxia – the infected RBCs adhere[13] to the vascular endothelial cells resulting in tissue anoxia, hypoglycaemia and lactic acidosis. This is especially true in the case of Plasmodium falciparum infection. It can also result in leakage of blood, protein and tissue fluid. The result of the above pathological purposes causes failure of organ system in which it occurs (liver, heart and kidney).

CLINICAL FEATURES:

Incubation period is the time interval between the infection and the onset of clinical symptoms or signs. The duration is variable for each species of malaria,

1) Plasmodium vivax – 12 – 17 days

2) Plasmodium ovale – 16 – 18 days

3) Plasmodium falciparum – 9 – 14 days

4) Plasmodium malariae – 18 – 40 days

The incubation period is subjected to change i.e., increase in case of a patient having partial immunity to the parasite or had incomplete chemotherapy[11].

UNCOMPLICATED MALARIA:

The classical presentation of a malarial fever is, child having paroxysms of fever, in between the febrile periods child shows relative wellness with mild fatigue.

Paroxysms: – each paroxysm coincide with the rupture of RBC releasing the schizont. This paroxysm of fever has three stages ie hot

stage, sweating stage, cold stage[8]. On an average each episode of paroxysm may last for about 8 to 12 hours. The paroxysm intervals vary with the species of malaria, Plasmodium vivax lasts 48 hours, Plasmodium malaria last 72 hours, Plasmodium ovale lasts 48 hours, Plasmodium falciparum less apparent occurs in mixed infection.

Non-specific signs/symptoms: – fever, chills and rigours, sweat, myalgia, abdominal pain, vomiting, pallor, diarrhoea, jaundice[11].

COMPLICATED/ SEVERE MALARIA:

As already mentioned the blood stage parasites are responsible for clinical manifestations in uncommitted malaria as well as the complicated form. Hence the parasitaemia of greater than 5% causes symptoms consistent with complicated severe malaria. Plasmodium falciparum is the most common reason for complications.

The clinical features to say severe malaria[11] are the presence of

a) altered level of consciousness,

b) prostration,

c) multiple seizures,

d) respiratory distress,

e) icteric,

f) cola coloured urine indicating haematuria,

g) abnormal bleeding,

h) severe pallor

i) pulmonary oedema

CEREBRAL MALARIA:

Plasmodium falciparum forms the most common cause of cerebral malaria, Plasmodium vivax rarely causes this entity.

This complication of Plasmodium falciparum occurs in persons with low level of immunity against the disease. Hence it occurs in young age group and adults living in areas of low transmission.

WHO defines cerebral malaria[11] as follows:

a) after seizure in the child does not regain consciousness of greater than 30 minutes; if other causes of encephalopathy like bacterial and viral encephalopathies[15] are ruled out.

b) evidence of Plasmodium falciparum in the peripheral blood smear examination[15].

Pathology of human cerebral malaria.

The knobs that are formed in RBC infected with Plasmodium falciparum adhere to the walls of the vessels. These knobs are formed by HRP 1 and 2. This leads to obstruction of the cerebral microvasculature resulting in small, petechial haemorrhages present over the white matter, the grey matter is always spared.

DURCH'S GRANULOMA:

At the site of microvasculature obstruction, ischaemia results and small haemorrhagic foci is formed. It is surrounded by glial cells[15]. There is an increase in the metabolic demands of the brain sends in addition to brain cells there are infected RBCs requiring glucose. This leads to increase in the cerebral blood flow[11] and a result there is also an increase in the intracranial pressure.

Coma in malaria is hypothesised to occur as a result of cytokines mediated nitric oxide release which act as a inhibitor of neurotransmission in the brain.

CLINICAL FEATURES:

The child presents with altered level of consciousness which ranges from drowsiness, confusion to coma.

Physical examination reveals the temperature of 106 -108 degrees Fahrenheit with seizure or muscle twitch or rhythmic movement of head and extremities. Fundoscopy[12] reveals retinal haemorrhage with unequal dilated pupils and other signs of upper motor neuron lesions are seen.

Lumbar puncture if done reveals increased intracranial pressure, normal glucose/protein concentration. The EEG remain normal.

Once treatment is started at the earliest recovery is generally complete. Delay in the treatment increases the risk of morbidity and mortality. Some children recover with sequelae such as aphasia, mental retardation hemiparesis, ataxia[11].

HEMATOLOGICAL ABNORMALITIES:

1) Anaemia: – the anaemia encountered in malaria is a normocytic normal chromic anaemia. There is no elevation of reticulocyte count. This anaemia is the result of haemolysis of infected cells, sequestration of the spleen, this erythropoiesis, Blackwater fever[11].

2) Low platelet count: – this results from mainly due to infection with Plasmodium falciparum.

3) DIC[11]: – it results from activation of coagulation by the pro-inflammatory mediators present in the blood as well as the infected RBCs.

4) Hypoglycaemia: – hypoglycaemia in malaria results from three possible predisposing factors,

   a) children

   b) pregnant woman

   c) Quinnine therapy

The act at various steps of the glucose utilisation like inhibition of gluconeogenesis, excessive glucose utilised by the parasites[11], activation of insulin secretion by quinine[12].

Hypo glycaemia causes a decrease in the sensorium of children as often confused with cerebral malaria. Hence identification of cerebral malaria induced hypoglycaemia and infection induced altered level of consciousness becomes of prime importance. The differentiation is not possible clinically hence only repeated blood sugar monitoring can solve the issue.

LACTIC ACIDOSIS:

The result of microvasculature obstruction by parasitised erythrocytes causes tissue anoxia as discussed earlier. This forms the major route for formation of lactic acid and the clinical condition lactic acidosis.

The measurement of plasma bicarbonate[12] and lactate concentration form the objective way of measuring the degree of lactic acidosis.

Other sources of lactate is the lactate produced by the malarial parasite and hepatic and renal failure which fails to clear the normally produced lactate[12].

BLACK WATER FEVER:

Intravascular haemolysis occurring due to malaria especially Plasmodium falciparum can be significant enough to produce a condition called Blackwater fever. It clinically presence with haemoglobin in patient with malaria. Predisposing factors are,

1) G6PD deficiency on quinine therapy.
2) Child receiving quinine,
3) G6PD[11] deficiency patient receiving oxidant drugs.

Blackwater fever can be simply told as an indicator of sudden intravascular massive haemolysis. It need not indicate any specific disease. It mostly seen in the malarial infection due to falciparum.

ACUTE RENAL FAILURE IN FALCIPARUM:

Acute renal failure is a feature of complicated malaria often seen in adults than children. There are two types of acute renal failure ie it can occur as an end result of multiple organ dysfunction syndrome or it can be a isolated event.

Acute renal failure occurring as an isolated event as a better prognosis than the one presenting as a part of the systemic event. The presentation of acute renal failure in malaria is an acute tubular necrosis. Very few cases develop glomerulonephritis[12].

MALARIA IN PREGNANCY:

In pregnancy, the placenta exhibits an adhesion receptor namely the chondriotin sulphate a on the surface of the placenta. The parasitised RBC gets attached to the placenta and impair the blood flow to the fetus.

The manifestation of the disease in the baby depends on a few factors such as the transmission intensity, and the immune status of the individual patient.

In areas of high transmission, the mother would have had high level of acquired immunity hence the disease does not manifest and remain asymptomatic in the mother as well as the fetus since passive transfer of immunoglobulins to the fetus occurs in pregnancy and breastfeeding. The anaemia caused by the haemolysis in the course of the disease can lead to fetal hypoxia and low-birth-weight[12].

In areas of low transmission, the level of acquired passive immunity is low hence the host living in this region are vulnerable to the complication of malaria. Here there are more incidence of spontaneous abortion, prematurity, stillbirth, low-birth-weight.

Maternal HIV also contribute to the increase in the fetal loss and congenital malaria since here again there is low acquired immunity. In this condition the patient is not able to mount an immune response.

PREVENTION:

WHO advises prevention of malaria during pregnancy by undertaking the following measures,

1) use of insecticide nets of long-lasting type,

2) use of proven to therapy with sulphadoxine – pyrimethamine,

3) early diagnosis and effective management.

MALARIAL HEPATITIS:

When the bile pigment synthesis reaches six times normal, the bilirubin rise is only 2 mg/dL. The liver has a very large reserve capacity so that it can compensate for this rise of bilirubin load.

Sometime severe jaundice is noted in the course of malarial infection, this cannot be purely due to haemolysis alone. Associated hepatocellular damage and cholestasis contribute to this rise of bilirubin.

In falciparum malaria, the liver enlarges and appears congested and dark brown pigmented. Kuffer cell hyperplasia along with dilated sinusoides and chronic infiltrates around the portal tracts.

The histopathological change predominant in the infected liver is Kuffer cell hyperplasia, malarial pigment Hemazoin[11] and congestion of the liver.

Clinical features	Laboratory tests
Age less than three years Decerebrate posturing Deep and prolonged coma Convulsions/ seizure. Haemorrhage within the retina. Absent corneal reflex. Organ dysfunctions.	Hyper parasitaemia greater than 5% haemoglobin <7gms, PCV<20% leucocytosis. Hypoglycoracchia CS of lactic acid greater than 6 mmol per litre. Low antithrombin 3. Increased plasma nucleotidase. B. Urea greater than 60 mg/dL . B. Glucose <50 mg % peripheral schizontemia S. Creatinine greater than 3 mg/dL

Table 2: Factors causing poor prognosis in cerebral malaria

CONGENITAL MALARIA:

Congenital malaria occurs in babies born of nonimmune mothers, infected with Plasmodium falciparum or Plasmodium vivax. The manifestations in the baby are seen around 10 to 30 days postnatal period.

The newborn shows signs and symptoms like fever, restlessness, pallor, jaundice, tiredness, loose tools, enlargement of liver, enlargement of spleen, bluish discolouration.

Congenital malaria is an important cause of abortion/premature birth/stillbirth/intrauterine death[11]. If there is no transmission to the fetus then it can result in IUGR.

TRANSFUSION MALARIA:

Many infections transmitted by blood transfusion of which malaria remains as one of the common causes. Two situations are encounter,

1) In an nonendemic areas, donor deferral along with screening of blood specific malarial immunoglobin eliminates trans mission.

2) In endemic areas identification of infected donors becomes tough. It can be made sensitive by specific questioning of the donor, looking into the seasonal and geography variation, if the donor is found positive antimalarials before transfusion might help.

NOSOCOMIAL MALARIA:

This transmission of malaria has been reported in a few cases and in a few settings, they are

1) The use of the same multidose heparin container among different patients in the hospital.

2) Reuse of single use saline flushes as resulted in nosocomial spread of malaria.

3) I V drug[14] addicts who share the same needle get the infection from their partners.

There is essentially no difference in the manifestation and management of malaria as with natural infection.

CHRONIC COMPLICATIONS OF MALARIA:

1) chronic anaemia,

2) failure to thrive,

3) vulnerability to infection,

4) specific syndromes – tropical splenomegaly syndrome, nephrotic syndrome, Burkitt's lymphoma, Endo myocardial fibrosis.

TSS SYNDROME (tropical splenomegaly syndrome):

This condition is also known as hyper reactive malarial splenomegaly syndrome, occurring in malaria endemic countries such as the sub Saharan Africa and the Indian subcontinent.

Repeated malarial infection leads to overstimulation of the immune system. When this occurs over a long period of time the mononuclear macrophage system gets activated and does the clearance of immune complex. The end result enlargement of spleen.

The spleen shows dilated sinusoides, marked erythro-phagocytosis, lymphocytic infiltrates. The peripheral smear is devoid of malarial parasite and turns out to be negative. The following features should be present to call tropical splenomegaly syndrome, they are

a) massive splenomegaly

b) marked increase in IgM[12] and antimalarial antibody,

c) enlargement of liver with Kuffer cell hyperplasia,

d) B-cell lymphocytosis.

All the marrow cells in all cell lines are decreased due to splenomegaly leading onto pan cyto penia.

TREATMENT:

Since continuous antigenic stimulus form the basis of the disease the treatment is directed towards the removal of the stimulus.

Chemoprophylaxis results in removal of the stimulus and return of the system to normal in three months[11].

In certain situations continuous stimulation can lead to lymphoproliferative disease.

ENDEMIC BURKITT'S LYMPHOMA

The malarial parasite produces pigment called haemozoin. Hemazoin is a breakdown product of haemoglobin after partial utilisation within the RBC by the malarial parasite.

This material released on RBC lysis enters into the circulation. It is taken up by the reticulo-endothelial system. The macrophage now becomes unable to mount an immune response. This leads to immunosuppression.

Ebstein barr virus[12] which remains under the control of the human immune system once immunosuppression occurs there is activation of the virus leading to Burkitt's lymphoma.

QUARTAN MALARIAL NEPHROPATHY:

Immune complexes formed as a result of Plasmodium malariae infection gets deposited in the basement membrane of the capillary.

Ultra microscopic finding indicate sub endothelial region deposits of basement membrane like material arranged in p plexiform manner, either focal or segmental with a nephritic[12] picture.

In areas of low transmission treatment is given as recommended in the guidelines.

Removal of spleen has no role in the management.

Three grades of nephropathy 1,2,3 are seen. Of these grade1 is granular pattern with good response to treatment. 2,3 poor response and the deposition is diffuse involving entire kidney.

DIAGNOSIS OF MALARIA

1) Microscopic examination: –

The time-tested investigation in the diagnosis of malaria is the peripheral smear examination using the light microscope. The peripheral blood examination identifies the merozoites and trophozoites in the blood. None of the other stages of the malarial parasite can be identified in the smear examination.

In certain situations the peripheral smear turns out to be negative, like partially treated or organisms are sequestered in the organs. In such situations the bone marrow examination yield to be fruitful.

Two smears are prepared, one thick and one thin. The thick smear helps in the quick scan for the identification of the parasite.

The thin[16] smear determines species type and also the percentage of RBCs which are infected. It also helps in the response to treatment.

Sample collection: –

The collection of blood for smear examination, the following precautions should be carried out

a) administration of antimalarial treatment, alters the morphology and hence the yield of the smear decreases.

b) ideal time for collection of samples for smear is after the febrile paroxysm[17], nephropathy shows no response to any form of drugs such as antimalarial, cytotoxic or steroids.

But this is not practically possible, so 4 to 6 hourly samples per day[16] for three consecutive days will be accurate. Negative in all these can be taken as absence of infection.

c) blood should be collected with EDTA and smear prepared within two hours of collection though ideally as early as possible.

Examination of blood film: –

In a suspected case of malaria, smear is prepared and examined under oil immersion 100 X objective. After examining at least hundred fields, if no parasite could be identified then it is concluded as negative. Three consecutive days sample should be examined.

Prognosticators in peripheral smear: –

The microvasculature burden of parasite is not represented by the peripheral blood parasitaemia. Though peripheral blood smear is negative

the microvasculature remains loaded with the parasite.

The schizont in the microvasculature rupture to release 32 merozoites. This results in an exponential rise of parasitaemia, high schizont count is an early marker of complicated malarial infection.

Account of greater than 10^ 4 parasites (schizont and trophozoites) high sensitivity/specificity of fatal outcome.

Plasmodium species	Stages found in circulating blood	Appearance of RBCs – SIZE	Appearance of RBC's – STIPPLING	Appearance of parasites – CYTOPLASM	Appearance of parasites –PIGMENT
Pl. falciparum	Trophozoites, gametocytes	Normal	clefts or dots seen called as Maurer's	Rings small and delicate with doubled or inside the rings	Gametocytes it appears black course and conspicuous
Pl. vivax	All: gametocytes schizonts trophozoites	Maximum size 1.5 –2 times, enlarged	Dots may be present Schuffner's dots	Appear light blue with irregular spreadout appearance amoeboid trophozoites	Golden brown inconspicuous
Pl. ovale	All: gametocytes trophozoites schizonts	Maximum size 1.25 – 1.5 times enlarged	Schuffner's dots may be present	Dark to medium blue rounded compact trophozoites	Dark brown conspicuous
Pl. Malariae	All: gametocytes trophozoites schizonts	Normal	Ziemann's dots rarely seen	dark blue with dense cytoplasm; band form trophozoites occasionally round compact trophozoites	Dark brown, course, conspicuous.

Table : The peripheral smear of different malarial parasite.

2) Quantitative buffy coat : –

Q BC is done on the principle of acridine orange stains the DNA content of the cell. The red blood cells are devoid of nuclear acids hence they are not stained. The parasitised RBCs containing the organism plasmodia contain DNA of the organism which gets stained with acridine.

The buffy coat is prepared on the principle of density gradient centrifugation of blood. The anti-coagulated blood centrifuged with 200 XG for 10 minutes. The cells are precipitated in the following order. The RBCs form the bottom layer followed by the WBCs about them and platelets above them. The RBCs containing organism are formed of the top layer of the RBC column. Using fluorescence microscopy the RBC containing parasite can be visualised[20,21,22].

The main drawback of the Q BC is that all cells containing the DNA[19] gets stained and hence differentiation from the parasitised RBC becomes important. The cells the stained are Howell jolly bodies seen in haemolytic anaemia, breakdown cells whose nucleic acid DNA mimics as parasites.

This method showed a sensitivity of 41% – 93% and a specificity of 52% to 93% for Plasmodium falciparum and non-Plasmodium

falciparum species[23,24]. This is one of the common test done in our hospital for the detection of malaria, the chief drawback is the delay in results.

RAPID DIAGNOSTIC TEST:

The presence of malarial parasite releases certain antigens into the blood. These antigens are detected by antibody coated strips in the mobile phase. This forms the basis of rapid diagnostic tests.

Principal: –

Monoclonal antibodies prepared against specific target antigens of malarial parasite are used. This antibody conjugated with selenium dye or gold particles forms the mobile phase. Nitrocellulose strips with monoclonal antibody act as the immobile phase. The mobile phase allowed to move[29] and captured by the immobile phase strip forming a visible line.

Based on the various targeted antigens multiple rapid diagnostic test are available in the market. The target antigens are HRP 2/PLDH/Aldolase.

a) Histidine rich protein 2:

This protein is exclusively produced by Plasmodium falciparum[25] in its gametogenic and asexual stages. It is a combination of histidine, Alanine, aspartate, with the major protein formed by histidine. Of the three types of HRP1,2,3 the second isomer is found universally in all Plasmodium falciparum species. The levels of HRP 2 clears in a period of 7 to 14 days[26] from the blood. Hence the test has certain limitations in the follow-up period. b) p (LDH) or

b) Plasmodium lactate dehydrogenase: –

Plasmodium lactate dehydrogenase is an enzyme produced by all the species of malarial parasite infecting man.

The isoforms of each parasite unique hence differentiation in terms of isoforms into different species types in malaria is possible. The isoforms have no cross-reactivity with the human isoforms.

One advantage of this test is P LDH is produced only by viable or living organisms present in the body and not by the dead parasites. This makes it possible to detect level of clearance and drug resistance[19] during the course of treatment.

c) Ex-Optimal test: –

Three lines are formed in the optimal test which identifies the Plasmodium lactate dehydrogenase enzyme. Two of the three lines are containing a pan lactate dehydrogenase detecting all the four types of malaria. One PLDH detects specifically Plasmodium falciparum malaria.

The isoforms of PLDH do not show any cross reactivity with other other parasites such babesiosis[28], leishmaniasis and other organisms. This improves the tests reliability and validity.

d) Plasmodium Aldolase: –

Plasmodium aldolase has a glycolytic function in the body of the parasite as well as binding function to actin, adhesion (thrombospondin related anomalous protein – TRAP). This plays an important role in protein binding and blocking the microcirculation. Antibodies against this enzyme provide protective immunity against infection[29].

e) Plasmodium glutamate dehydrogenase: –

The enzyme also has a role in carbon nitrogen metabolism. The enzyme galactose dehydrogenase provides oxidisable carbon source required for energy production as well as reduced electron carrier. It is

also an amino acid donor to other amino acids in subsequent transamination reactions.

Glutamate dehydrogenase enzyme is also produced by the living parasite and hence it can be used to detect the presence of viable organisms in the blood.

The disadvantages of the rapid diagnostic test which limits its utility are as follows:

1) not able to identify mixed infection

2) the test kits are not able to stage the parasite development level, limiting its utility in surveillance.

3) rapid diagnostic test being expensive limits its usefulness in large scale field studies.

4) the proper function of rapid diagnostic test depends on the temperature, exposure to high temperature results are affected. So transport rural areas care should be taken to prevent exposure to high temperatures.

5) the person has persistent antigen in the body the test shows positive. This condition is a result of incomplete treatment.

POLYMERASE CHAIN REACTION (PCR)

The PCR has the accuracy level of hundred percent to detect all species at all stages of the malarial parasite. The main disadvantage of the test is expensive equipments and the cost of the test. This PCR can replace microscopy[19] for research purposes.

Table : Comparison of microscopy with RDT

	Microscopy	Rapid diagnostic test
Requirements		
a) supplies	Blood, staining reagents	Blood collection
b) electricity	Preferred	Not necessary
c) equipments	Microscope	None
d) training	Trained technician	Minimal training
Performance		
a) subjectivity	High	Low
b) robustness	Average	High
c) labour-intensive	High	Low
d) test duration	60 minutes	20 minutes
Technical specifications		
a) threshold	5-10 parasite/microlitre	40-100 parasite/miclit
b) detect all species	Yes	No
c) quantification	Yes	No

MANAGEMENT[6]

a) In areas where Plasmodium is sensitive to chloroquine;

chloroquine a total dose of 25 mg/kg is given in this situation. It is given in the following order. Day 1 – 10mg/kg single-dose

day2 –10mg/kg single-dose

day3 – 5mg/kg single-dose.

Vivax: radical cure is achieved by adding primaquine 0.25 mg/kg per day for a period of 14 days.

Falciparum: primaquine 0.75 mg/kg stat dose for the sexual stages of the malarial parasite.

b) Chloroquine resistant Plasmodium falciparum:

artesunate – 4mg/kg od for three days d1, d2, d3

plus

sulfodoxime-pyrimethamine single-dose on day one.

or

artesunate 4mg/kg once-daily on d1,d2,d3

mefloquine 25mg/kg divided doses on day two, day three

or

Artemether 20 MG +120 MG Lumefrantine six doses bd on day1 ,2,3.

c) MDR Plasmodium falciparum:

quinine 10mg/kg per dose three times a day for seven days

plus

doxycycline 3.5mg/kg once-daily for seven days

(or) tetracycline 4mg/kg per dose four times a day for seven days

(or) clindamycin 20mg/kg per day twice-daily for seven days

If the patient develops quinine toxicity also called Cinchonism,

quinine 10mg/kg per dose three times a day for 35 days

(plus) tetracycline (>8 yrs) 4mg/kg per dose four times a day 10 days

(or) doxycycline (> 8yrs) 3.5mg/kg once-daily for seven days

(or) clindamycin 20 mg/kg per day twice-daily for seven days

Primaquine 0 .75 mg/kg single-dose for children greater than one year to destroy the sexual stages in the falciparum malaria.

d) ACT – artemisinin combination therapy

There is a very rare chance of failure with ACT therapy for 14 days.

In case of an event of failure to chemotherapy it should be confirmed by blood smear examination. The patient should be enquired if he had vomited the drug or he has missed out the drugs. In the case of failure of treatment retreatment with ACT is done.

e) NAMP regimen for complicated/severe malaria:

1) quinine salt:

Loading dose 20mg/kg in 10ml/kg of 5% dextrose over four hour followed by, maintenance dose – 10 mg/kg for two hours repeated every 8 hrs.

If the patient is able to swallow then changeover to oral quinine Oral quinine 10mg/kg eight hourly for seven days plus tetracycline or doxycycline or clindamycin for seven days.

I.V. Access is not available then, quinine can be given IM at the same dose as IV on the Antero lateral thigh. This can also be given when

quinine cannot be given IV. IM quinine is diluted in normal saline 60 – 100mg/kg along with tetracycline/doxycycline/clindamycin.

2) artesunate: –

2.4mg/kg IV at 12, 24, 48, 72 hours for seven days

if there is no vomiting them daily same dose given orally along with Tetra, Doxy, Clinda.

(Or) artemether:

3.2 mg/kg IM given as a loading dose followed by 1.6 mg/kg OD for six days.

If there is no vomiting, daily oral dose along with any one of the three Tetra/Doxy/Clinda for seven days

SUPPORTIVE MANAGEMENT[6]:

1) cardiopulmonary cerebral assessment should be done for all cases of malaria (complicated/severe) to identify shock.

2) antimalarials drug should be administered without delay since delay can cause progression of disease even in a short span of two hours.

3) aspiration can be prevented by NG tube insertion if ALOC present.

4) ventilator support if needed.

5) antiepileptic drugs as required for the situation.

6) threat febrile paroxysms.

7) blood transfusion/exchange transmission has indicated

8) supportive care for acute renal failure

9) measure parasitaemia from time to time.

CONTROL:

The spread of malaria at the community level can be blocked by the following measures[10].

a) intervention through community participation.

b) vector control: mosquito breeding increases the vector density this can be reduced by certain measures,

insecticide spraying such as malathion, ultralow volume fogging.

Anti-larval measures such as Gambusia, lebister reticularis which feeds on the mosquito can be used.

Oiling the stagnant water so that oxygen to the organism is cut off.

Proper disposal of waste water to prevent stagnation and mosquito breeding.

Self protection done by using nets, repellents[5] etc..

b) early diagnosis and treatment: – the next step in the control of transmission through the vector is to block infected persons from infecting the mosquito so that they do not spread the disease.

CHEMOPROPHYLAXIS[11]

Individual visiting endemic areas are at risk of acquiring malaria and on return to their state there is a chance of spreading the disease. Chemoprophylaxis using antimalarials one week before to 4 weeks after leaving the area prevents spread .

Chemoprophylaxis:

If chloroquine sensitive, consider use of chloroquine 5mg/kg weekly along with or proguanil 3mg/kg daily.

If chloroquine resistant, consider use of mefloquine 5mg/kg weekly if unavailable along with Doxy 2mg/kg. Daily

DRUG RESISTENT[34]:

Resistance to chloroquine is mainly noted in malaria caused by falciparum. The resistance can be divided into four grades they are as follows.

S: sensitiv E: if there is no parasitaemia on day six of treatment and the absence of recrudescence or date 28

R1 : low-grade resistance: recrudescence in the past two weeks is also called early and if it occurs second to fourth week's call.

R2 : high-grade resistance: the parasite density is clearway the spleen. Parasite density of greater than 75%, but it could not be completely cleared.

R3: when the is no clearance of parasitaemia on completion of treatment at 48 hours and thereafter.

MALARIAL VACCINES

Vaccines are an integral part of preventive medicine, but as far as malarial infection is concerned there are certain limitations. These limitations are discussed below.

The malarial parasite undergoes a series of stages in its development ie complexity in its life cycle. At each stage the parasite undergoes antigenic variation with deffers the body and us from producing a vaccine which can specifically hit the target.

The focus of vaccine lies on the three stages of development that is

a) sporozoite: this is the infective stage of the malarial parasite from mosquito. Blocking this stage prevents man getting infect.

b) merozoites: erythrocytic invasion is done by these merozoites, blocking them can about the erythrocytic phase of the malarial parasite.

c) gametocyte: an effective vaccine against the gametocytes when the infection of the mosquito hence preventing spread.

Cocktail vaccine:

Multiple antigens are involved in the life cycle of malaria hence a single vaccine against a single antigen might not prove to be effective so it has been hypothesised that vaccine against multiple epitopes in a single vaccine is required. This type of vaccine is called the cocktail vaccine.

Vaccines available:

a) MSP1 and MSP2 vaccine: merozoites surface antigen 1&2

b) erythrocyte binding antigen 175

c) gametocyte antigen Pfs 25[35]

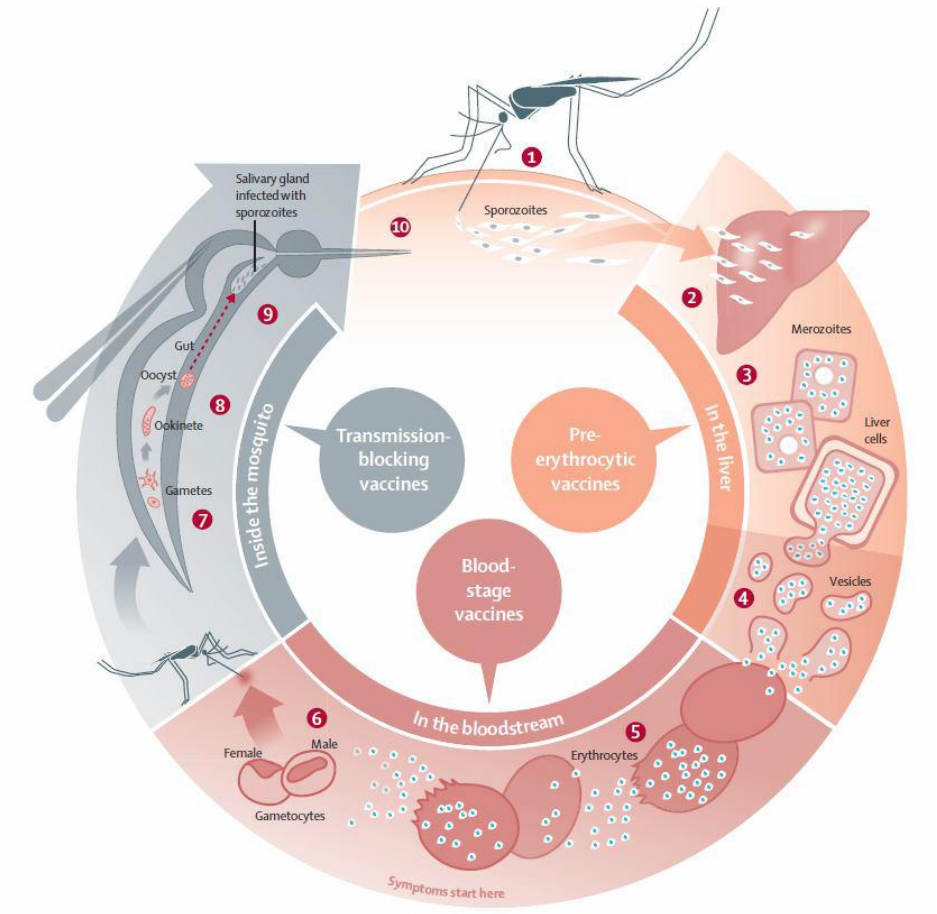


Fig 3*:* Sites in the malaria life cycle that could be interrupted by VACCINE[2]

1) The life cycle of the malarial parasite starts at the injection of Plasmodium species during the blood meal of the mosquito (sporozoite).

2) Sporozoites reach the liver in a few minutes time. Multiplication of the sporozoites takes place for the next 7 to 10 days, during the period the patient remains asymptomatic.

3) After the development in the hepatocyte the merozoites are released in the form of vesicles. The merozoites reaches the lung capillaries breaks the vesicles freeing the merozoites into the circulation.

4) Merozoites enter the RBCs and multiply asexually, on completion multiplication the RBCs lysis and the parasites are released. They are ready to infect fresh RBCs.

5) In some RBCs multiplying by asexual means stops and gametocytes are produced which mature to form gametes.

6) Gametocytes are ingested by the mosquito and further fusion and development occurs in the stomach of the mosquito.

7) Ookinetes burrow the midgut wall of the mosquito and forms oocyst, in the oocyst several hundred sporozoites are developed and burst to release.

8) The sporozoites released from the that enter the blood and through the circulation they reach the salivary gland of the mosquito. They reside here and during the blood meal they enter the circulation of their intermediate host.

METHODOLOGY

SELECTION OF CASES

The study conducted on children 1yr to 12yr with clinical features of malaria meeting the inclusion and exclusion criteria in op/ Ip visiting our paediatric department

INCLUSION CRITERIA

- Children 1-12 year age with clinical signs of malaria
- Clinical signs- fever with chills and rigors, pallor, splenomegaly

EXCLUSION CRITERIA

- Age <1 yr or >12 yr
- Already on treatment, partially treated in past 4 weeks
- Children having renal, liver, lung disorders

METHOD OF STUDY

1) COLLECTION OF SAMPLE : About 160 cases attending op/ip cases in paediatric department, patients with clinical features of malaria meeting the inclusion and exclusion criteria form the study sample. Two ml of venous blood drawn under strict aseptic precautions in a sterile edta tube.

PERIPHERAL SMEAR STUDY:

One thick blood smear and another thing blood smear were prepared from the sample collected.

A drop of blood is placed on the middle of the glass slide. The spreader usually the corner of another glass slide is used. The spreader converts the drop of blood in half an inch square and then allowed to dry. Roughly the spreading is done to the other side is partly seen through the blood sample of smear.

A small drop of blood is placed at one end of **the glass slide**. A clean glass slide is used as a spreader. The edge of the glass slide is then kept at 45° angle with the slide containing a drop of blood on its side. The blood spreads between the edge and the plate of glass, the glass slide is lowered to 30° angle and pushed. The spreader is pushed till all the drop of blood is exhausted. The smear is thus prepared and allowed to dry.

Both the glass slide one thin another thick are labelled. The thin slide is fixed with methanol.

Fixing the smear: – the thin smear is dipped in methanol for five seconds to get fixed. The thick smear is not fixed. Staining the slide: – both the slides are stained with Leishmann's stain. Before staining the thick smear dehaemoglobinised using distilled water. Then dried smear is allowed to stand.

With Leishman's stain for 30 seconds. The distilled water is allowed to remain over the slide for about 10 to 15 minutes. The slide is prepared is held under the tap water for a free flow of water over it. The slide is then dried by placing it in a slanting position, before placing to dry the back of the slide is rinsed with wet cotton.

After the above procedure the thick and thin smears are loaded on a light microscope. The smears are examined under the 100 X objective. Multiple fields are searched in the thick smear for parasites.

The entire procedure is done in 5 to 6 minutes, on average hundred fields are examined. The result is given negative if no parasite are seen at the end of examining hundred fields for five minutes.

The species of parasite is identified using the thin smear, the stage of development can also be identified using the thin smear. The number of parasites per cubic millimetre is found using the thick smear, this is not done for all cases that are examined.

RAPID DIAGNOSTIC TESTS:

This is an immuno-chromatographic method to identify the malarial parasite using the HRP 2/PLDH antigens present in the human blood during infection. This is done using a commercial kit from SD bio line.

Principal of the test: – HRP 2/PLDH as already explained are antigens detected.

The monoclonal HRP2/PLDH antibody coated in the malarial strip. The appearance of test lines indicate positive result. The absence of along with the control indicate the card is invalid. The appearance of control line alone indicate the card is valid but the test is negative.

Materials used: –

1) a rapid test kit card.

2) assay the diluent.

3) micro pipette.

Procedure: – the card is stored under room temperature. High storage temperatures alters the results. The card is placed on a horizontal flat surface, five Micro drops of blood is collected from the sample taken for smear examination using the sample collector which comes along with the kit. The sample of blood is placed in the small micro well of the card. Four drops of diluent is added into the larger on the card and allowed it to stand for 20 minutes. As the mobile phase passes through the immobile phase the following results are interpreted.

Interpretation: –

Negative – only the control line appear and the PF and pan lines does not.

Positive – appearance of lines at T1 or T1 and T2 – Plasmodium falciparum

Appearance of control line and T2 line – Plasmodium vivax

Invalid – even the control line does not appear, the card is invalid

Statistical analysis

The test results are obtained in the form of numbers and percentages. Chi-square test was done for categorical data and their relations with malaria positivity was noted. The sensitivity and specificity, negative predictive value and positive predictive value all pointing towards the diagnostic validity of the test was performed, To compare peripheral blood smear and rapid diagnostic test. The Kappa measure of agreement was applied to find of the correctness of the correlation. The P value less than 0.005 was considered statistically significant. All operation done using SPSS for Windows version 6.

Fig 4: Anopheline Vectors Of Malaria

anopheles stephensi

anopheles gambia

Fig 6: Pl.falciparum gametocyte in thin blood smear.

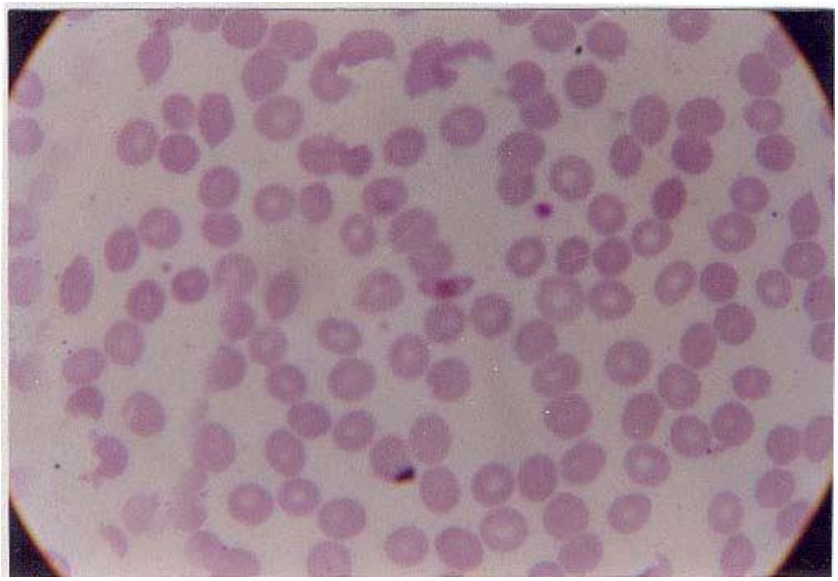


Fig 7: Pl.falciparum ring stage in thin blood smear.

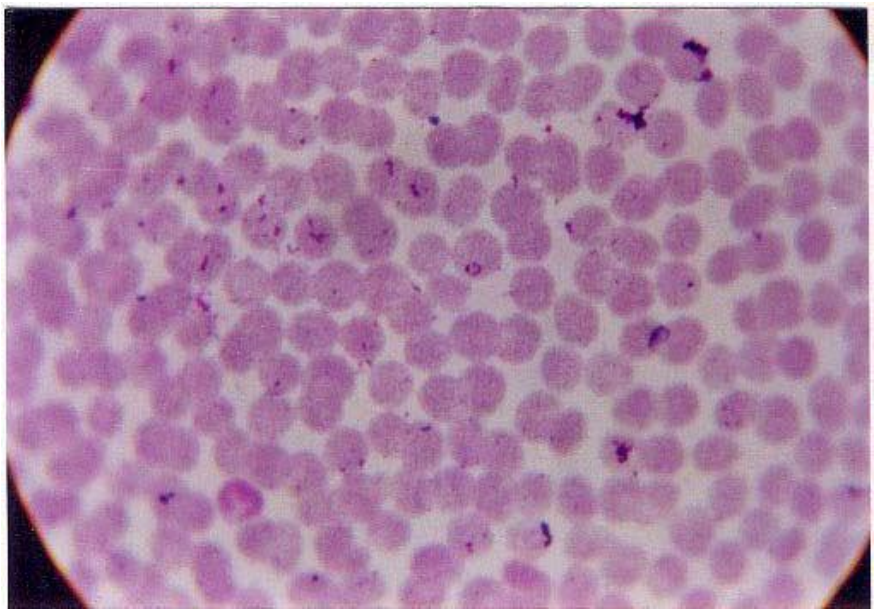


Fig 8: Plasmodium trophozoites in thick blood smear.

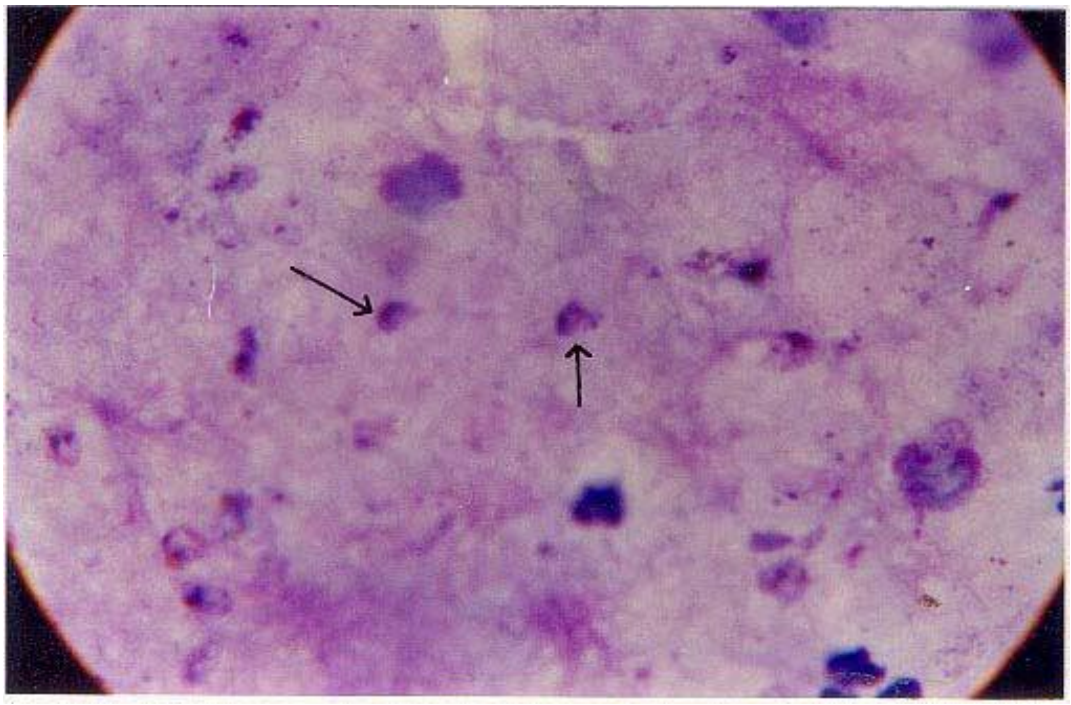


Fig 9 : RAPID MALARIA TEST KIT (HRP2/pLDH)

Fig 10: Test procedure done with rapid diagnostic test

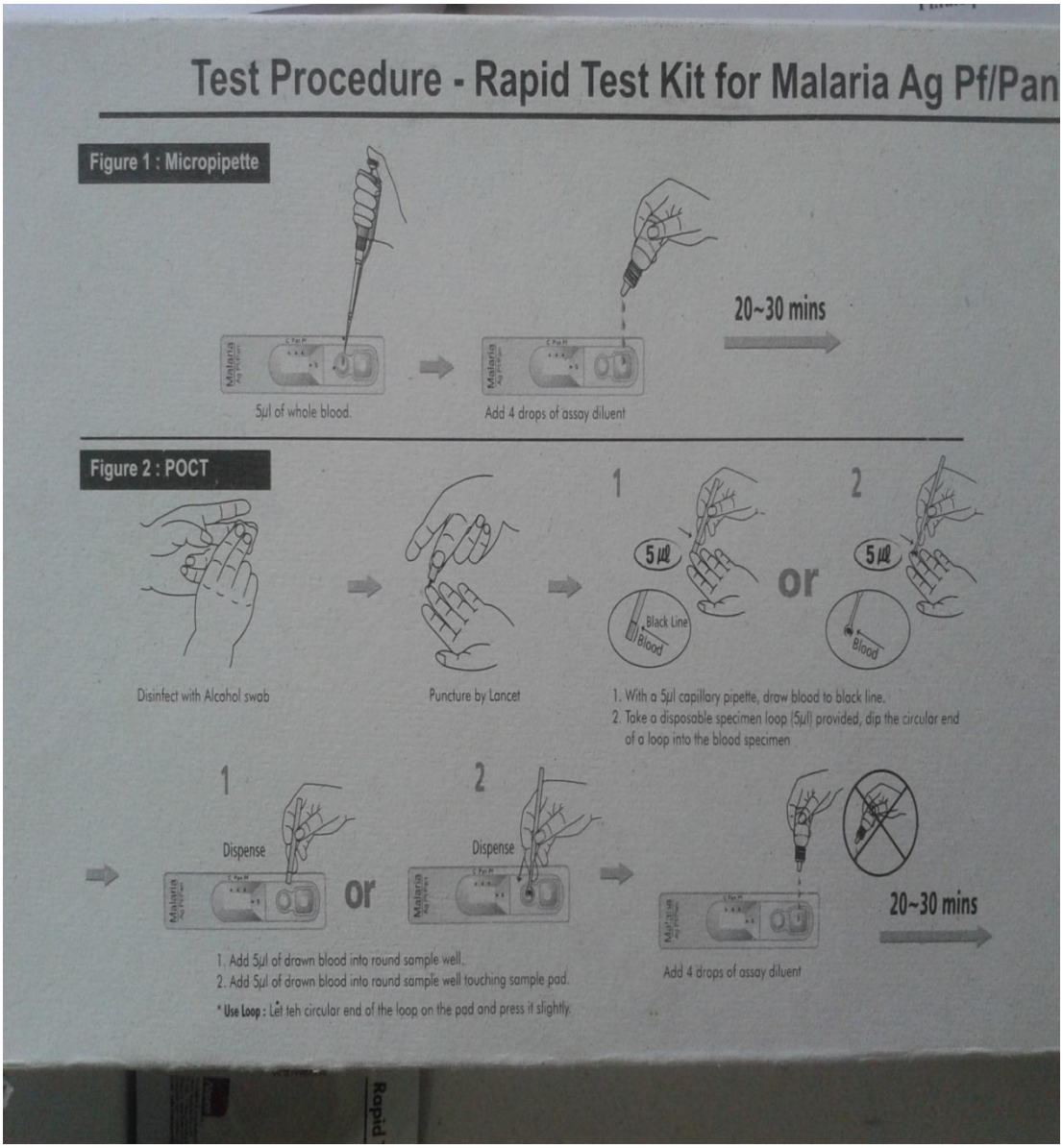


Table 6 : Distribution of positive cases by peripheral smear and HRP2/PLDH

	Number	Percentage	Number	Percentage
Positive Cases	39	24.4		
Negative Cases	121	75.6		
Total	160	100		
Plasmodium vivax			28	71.8
Plasmodium falciparum			11	28.2

Of the suspected cases of malaria 39 cases were through positive and 121 cases were through negative by peripheral blood smear and malarial rapid diagnostic test. This constitutes 24.4% and 75.6% positive and negative respectively by both the tests. 28 cases were plasmodium vivax and 11 cases were plasmodium falciparum.

Graph 1: Total positive cases distributed by either method

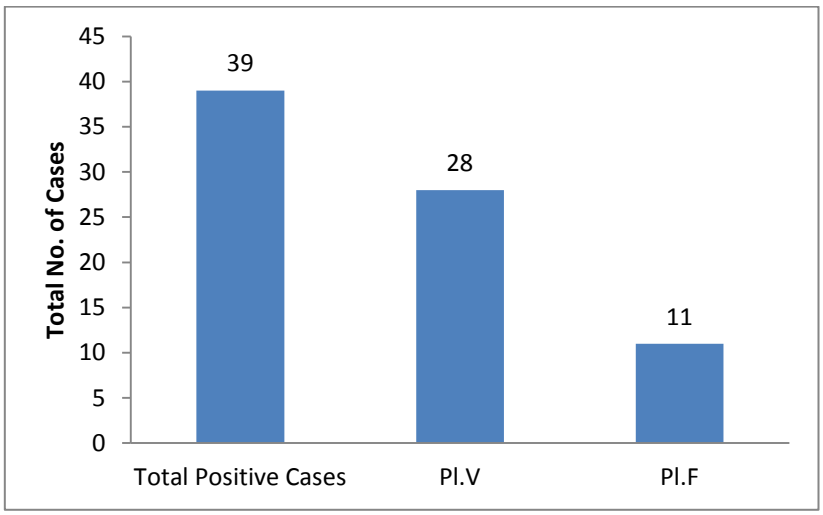


Table 7 : Gender Distribution of Malaria Positive Cases.

Sex	Total no of Cases	Positive Cases	Percentage %
Male	92	24	61.5
Female	68	15	38.5
Total	160	39	100

(X2= 0.34; P =0.56) (Non - Significant)

In the 39 cases, confirmed positive for malaria, male children constitute 15 (38.5%) and the female children constitute 24 (61.5%). There is no statistical significance between male and female sex wise incidence.

Graph 3: Distribution of Malaria Cases sex wise.

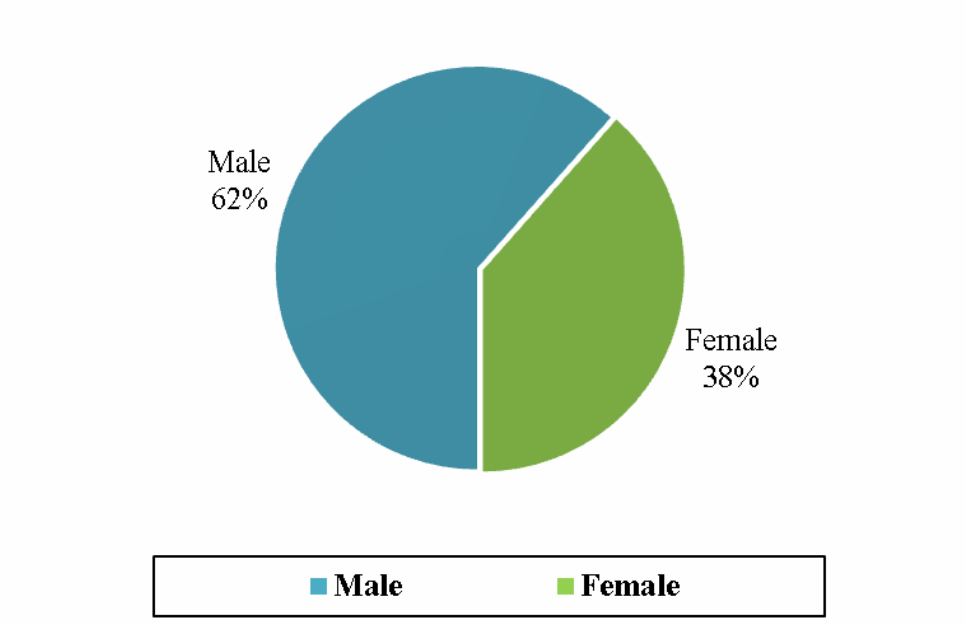


Table 8 : Symptomatic distribution of Malaria in Children

Symptoms	No of cases	No of positive cases	Percentage %	X2	P
Fever	160	39	100	-	-
Chills and rigors	77	20	51.2	0.58	0.75
Sweating	16	6	15.6	1.66	0.20
Headache	73	15	38.5	1.07	0.3
Pain abdomen	49	14	35.9	0.68	41

Of the 39 cases of malaria positives, fever was seen in all cases. Statistical analysis did not reveal any other symptoms to be consistently correlating with the disease. No cases had or showed any symptoms of severe malaria.

Graph 4: Symptomatic distribution of Malaria in children

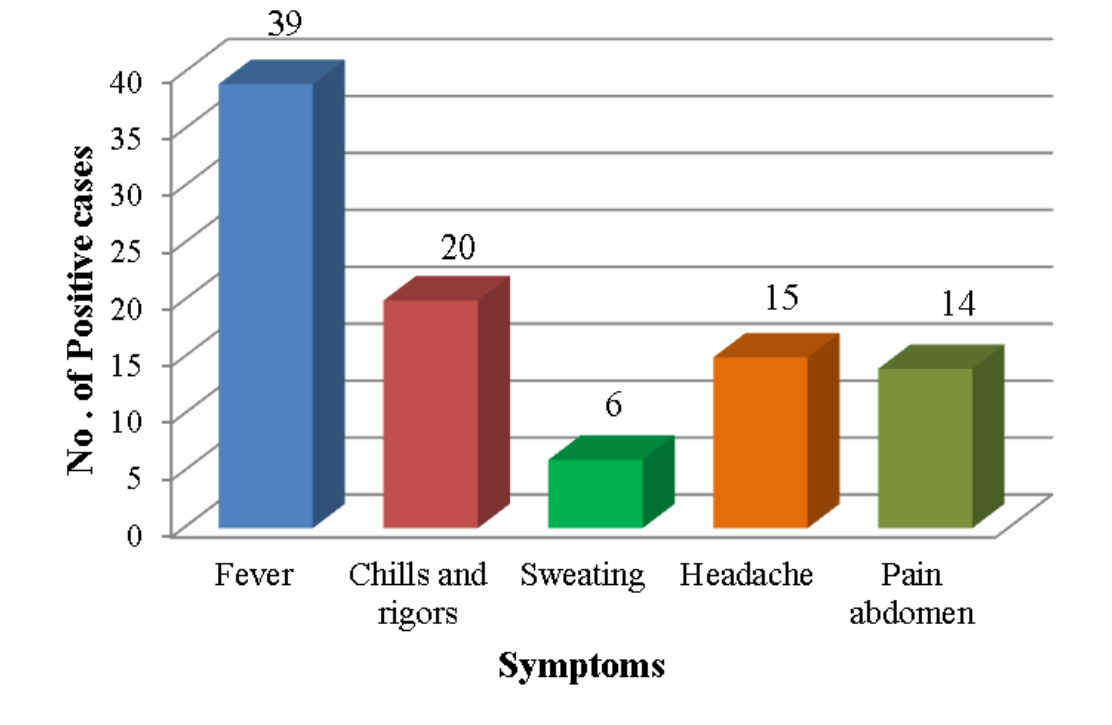


Table 9: Signs in Children with Malaria.

Signs	Total no of cases	No of positive cases	Percentage %	X2	P
Pallor	77	25	64.1	5.27	0.02(HS)
Splenomegaly	128	35	89.7	3.06	0.08(NS)
Hepatomegaly	126	29	74.3	0.59	0.44(NS)

Among the signs pallor was seen in 25 (64.1%) of cases being statistically significant (P<0.02). Spleen 35 (89.7%) and liver 29 (74.3%) in the positive cases.

Graph 5: Signs in children with malaria

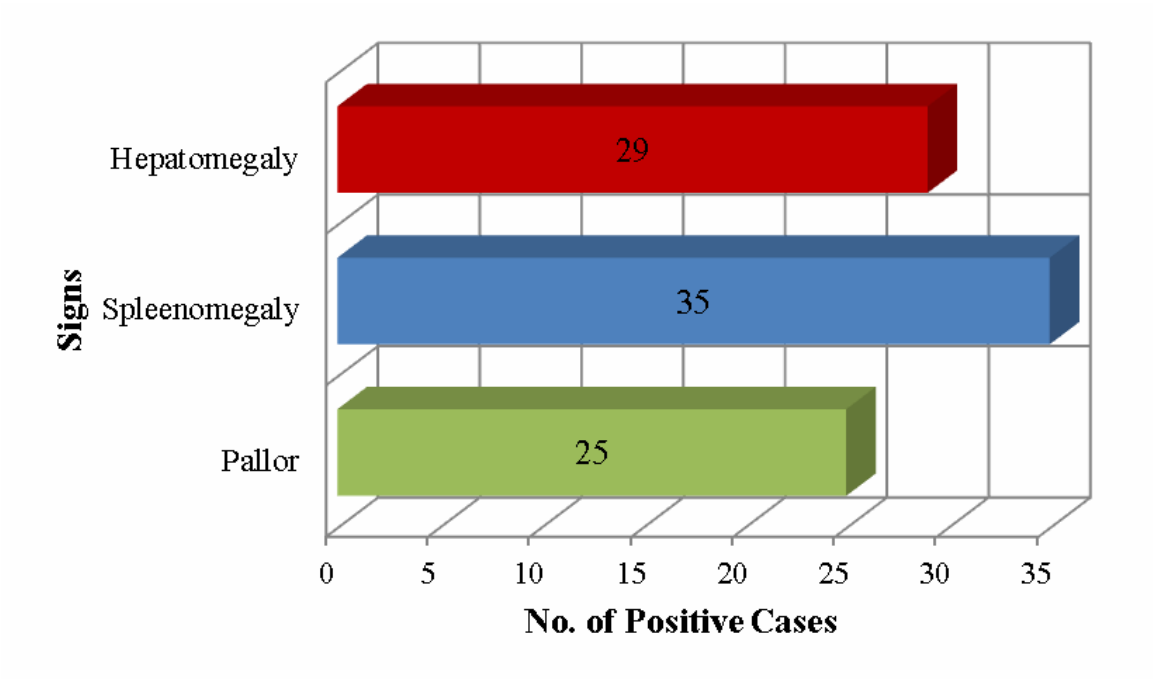


Table 10 : Weight correlation of Malaria cases

Wt. for age%	Total cases	Positive cases	Percentage %
71%-80%	56	12	30.8
>80%	104	27	69.2
Total	160	39	100

X2=0.4, P= 0.52 NS

There was no significant correlation in weight and incidence of malaria in our study. Greater than 80% weight group were 27 cases, 71%-81% were 12 cases.

Graph 6: Weight correlation of Malaria cases

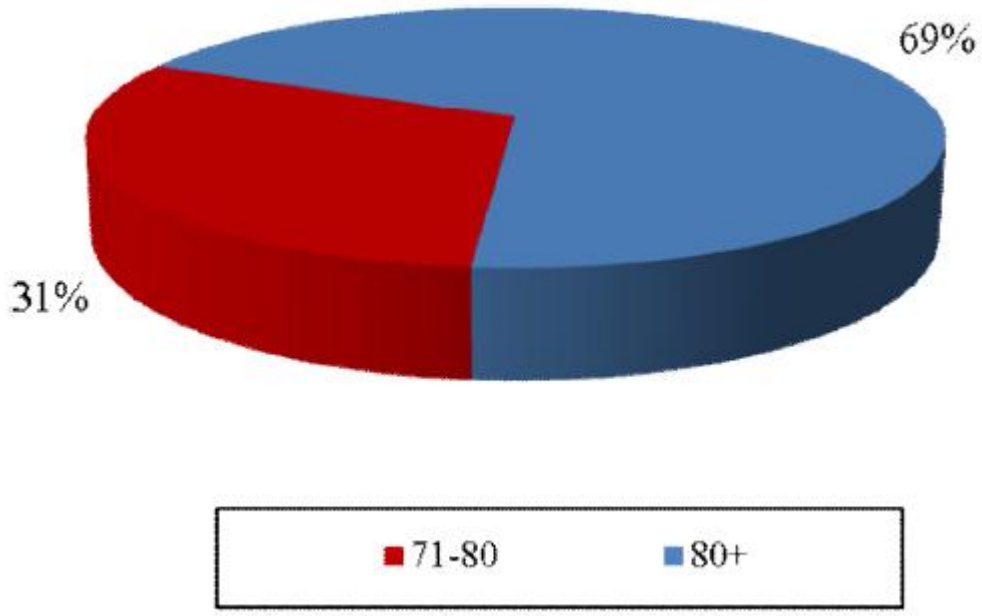


Table 11: Hemoglobin in children with malaria

Hemoglobin%	Total cases	Positive cases	Percentage%
6-8	81	11	28.2
8-10	55	16	41.0
>10	74	12	30.8
Total	160	39	100

X2=5.44, P= 0.05 HS

The hemoglobin percentage revealed a significant difference with 16 cases ie., 41% in the 8-10 g % range, 12 cases >10 g % range and about 11 cases 6-8 g % group.

Graph 7: Hemoglobin in children with malaria

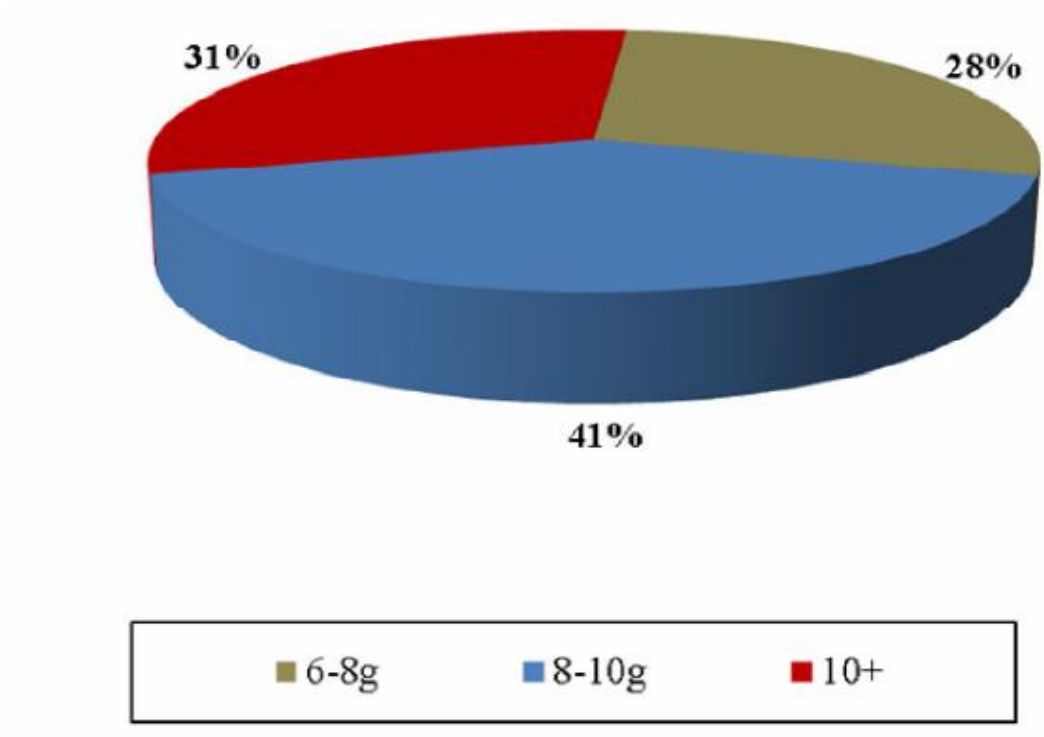


Table 12 : WBC levels in malaria cases.

WBC count (per cmm)	Total no of cases	Positive cases	Percentage
<4000	30	4	10.2
4000-11000	99	30	76.9
>11000	31	5	12.8
Total	160	39	100

No significant difference was found in WBC count which was statistically significant. 13 cases fell into 4000-11000 range. 4 cases were less than 4000 cells.

Graph 8: WBC levels in malaria cases.

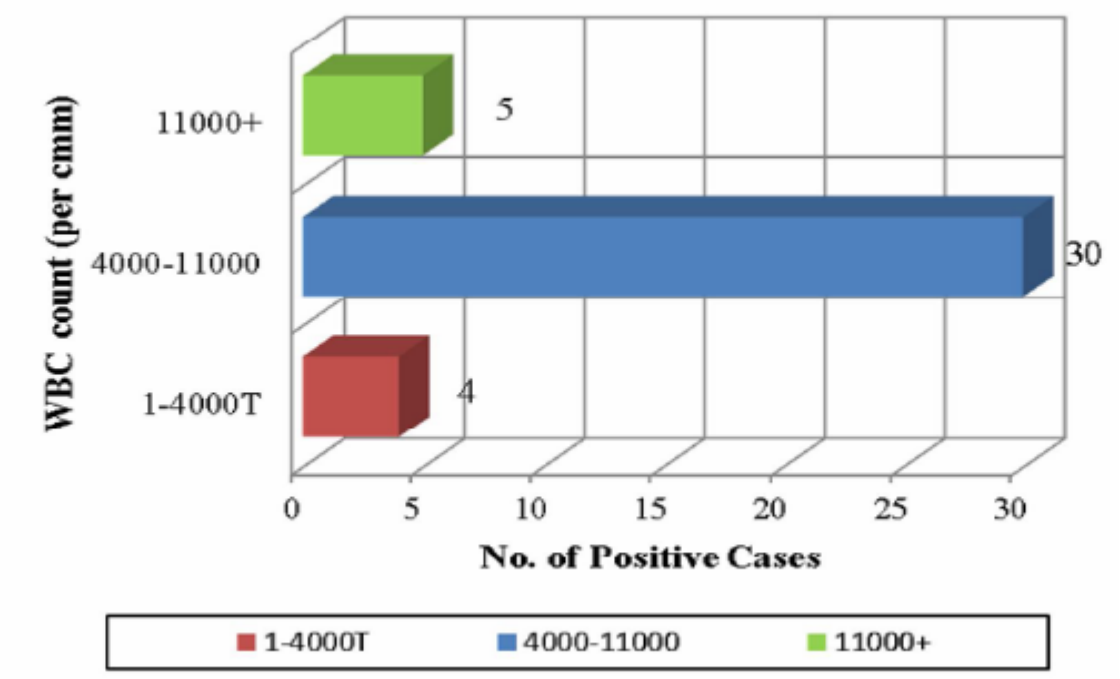


Table 13 : Monocyte counts in malaria.

Monocyte count%	Total no of cases	Positive cases	Percentage %
0-3	67	14	36
4-6	60	18	46
7-9	33	7	18
Total	160	39	100

X2=1.65, P= 0.44 NS

There was no statistical significance in the monocyte count between the cases of malaria. 46.2% cases had monocyte count of 4%-6%.

Graph 9: Monocyte counts in malaria.

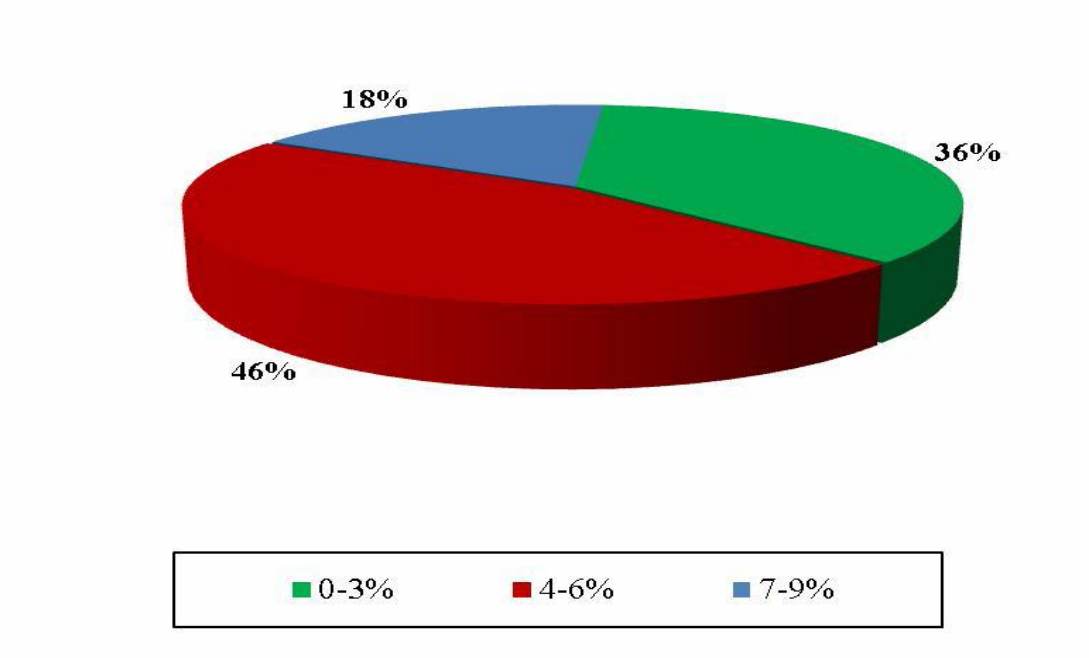


Table 14 : Platelet counts in Malaria

Platelet count (lakhs/cmm)	Total no of cases	Positive cases	Percentage %
<1.5	102	31	79
1.5-4.5	58	8	21
Total	160	39	100

There was a statistically significant correlation between platelet and malaria cases. 31 cases had counts less than 1.5 lakhs, 8 cases had 1.5-4.5 lakhs which constitute 79.5% and 20.5% respectively.

Graph 10: Platelet count in Malaria

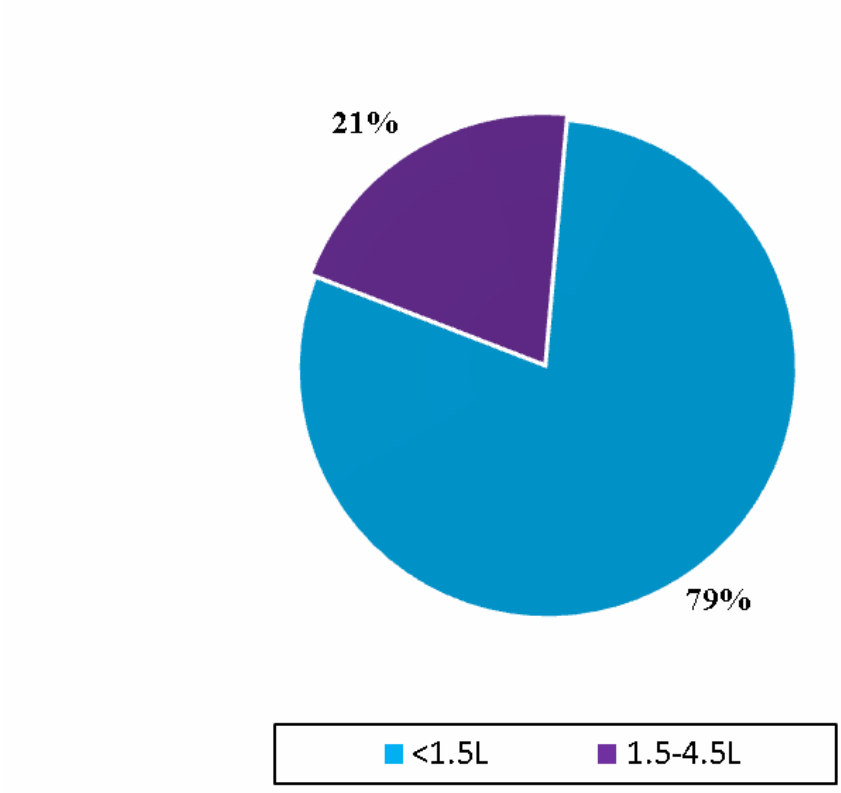


Table15 : Species of parasite by peripheral smear study

Species	No of cases	Percentage %
Pl.vivax	23	71.8
Pl.falcipaum	9	28.2
Total	32	100

It shows 32 cases positive for plasmodium vivaxin the peripheral smear study. 9 case plasmodium falciparum, which mount to 71% and 28% respectively.

Graph 11: Species of parasite by peripheral smear study

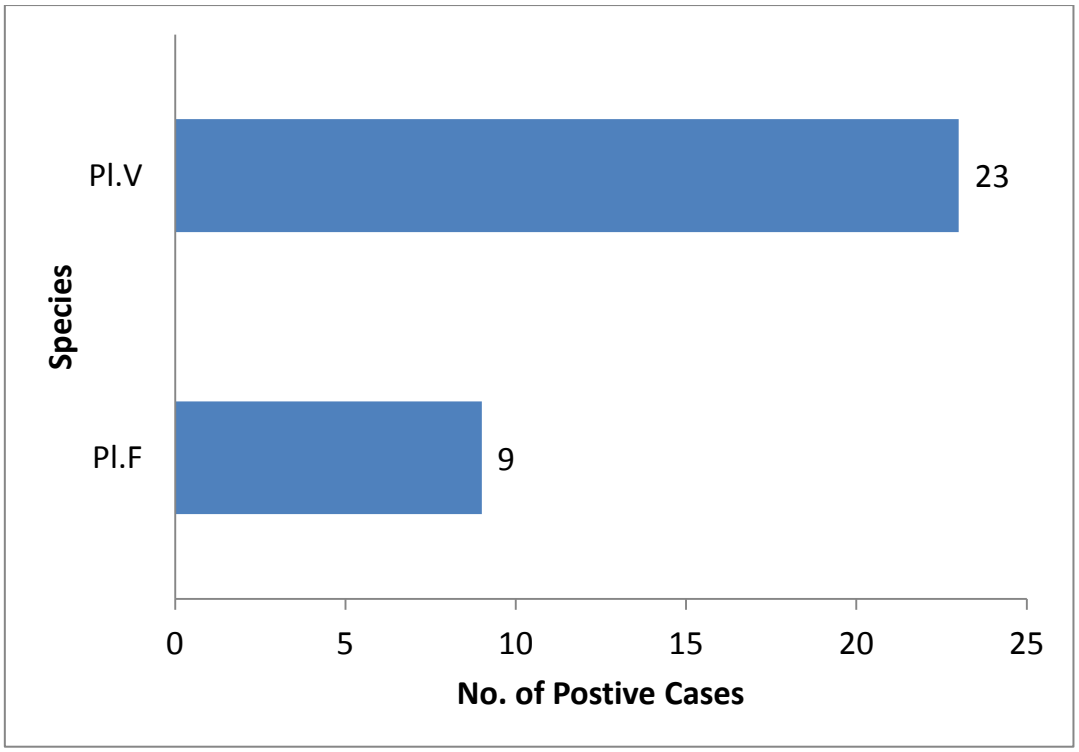


Table 16 : Comparison between the 2 tests in the diagnosis of malaria based on species

TEST	Pl.vivax	Pl.falciparum	X^2	P value
PBS	23	9	124.1	<0.001HS
HRP2/PLDH	26	11	149.3	<0.001HS

Both the above tests reveal that plasmodium vivax are more when compared to plasmodium falciparum. The test was statistically significant. The total number of plasmodium vivax and plasmodium falciparum was 28 and 11 by both the above tests.

Graph 13: Comparison between the 2 tests in the diagnosis of malaria based on species

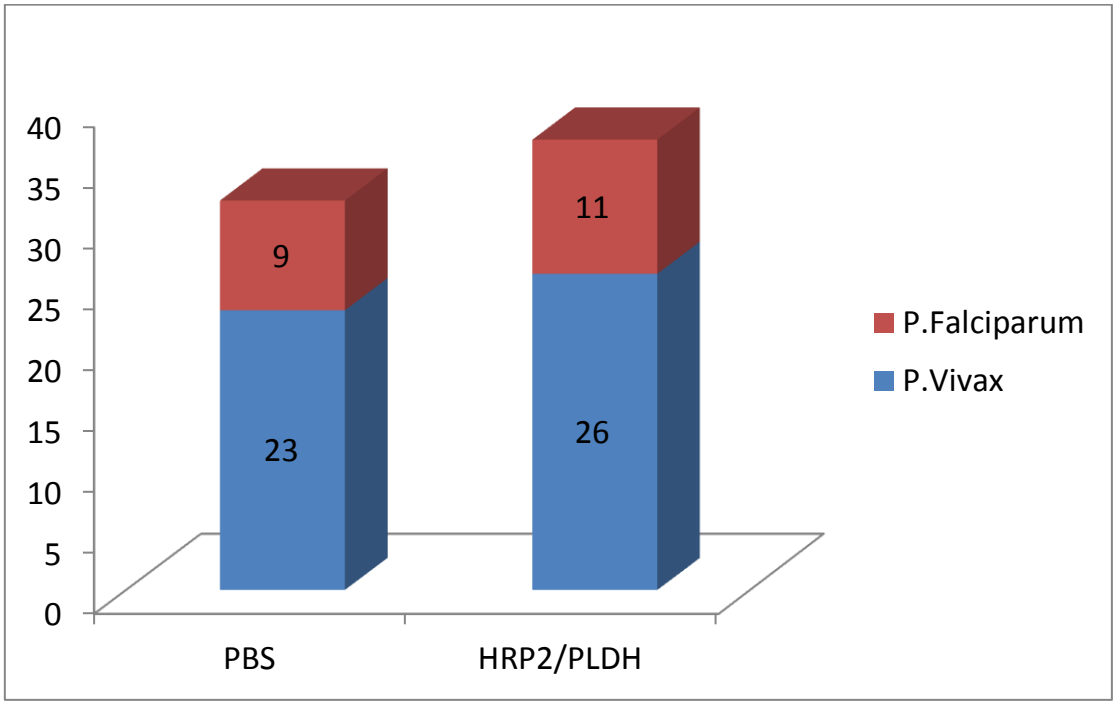


Table 17 : Correlation of HRP2/PLDH test with peripheral blood smears.

Plasmodium species	HRP2/PLDH Result	PBS result		
		Positive	**Negative**	**Total**
Pl. vivax	Positive	21	5	26
	Negative	2	132	134
	Total	23	137	160
	X2=111.2 ; P < .001 HS			
Pl. falciparum	Positive	9	2	11
	Negative	0	149	149
	Total	9	151	160
	X2=129.2 ; P<.001 HS			

Plasmodium vivax was positive in both the tests were 21 cases. The remaining 5 cases of the 26 cases positive for plasmodium vivax were shown by HRP2/PLDH kit test. 2 cases negative in the card test were shown positive by peripheral smear. Comparing the difference, it is proved to be statistically significant.

Both methods similarly were positive for plasmodium falciparum in 9 cases. Peripheral blood smear was negative in 2 cases which were identified by rapid diagnostic tests. Applying statistical analysis it revealed to be highly significant.

Table 18: Correlation of Peripheral blood smears with HRP2/pLDH test.

HRP2/PLDH Result	PBS result		
	Positive	**Negative**	**Total**
Positive	30	7	37
Negative	2	121	123
Total	32	128	160

From this comparison tables it is well understood that HRP2/PLDH is sensitive, specific with a percentage of 93%, 94% respectively. The positive predictive value, negative predictive value, and diagnostic efficacy was 81.1%, 98.4%, and 94.4% respectively.

DISCUSSION

This study "The role of immune chromatographic antigen detection test assay in the early diagnosis of malaria" was done in Institute of social paediatrics, Stanley medical College located in North Chennai area. During the study the children brought to the hospital within 12 years of age having fever were studied.

The incidence was more among children belonging to 9 to 12 year age group of which male children constituted 61.5% and female children that 38.5%. The total number of cases positive were 39 of which 24 cases were male children and 15 cases were female children.

In our study the symptoms most commonly encountered in children having malaria were 1) fever – 100%, 2) chills and rigors – 52%, 3) headache – 38% 4) sweating – 15% 5) abdominal pain – 35%.

On systemic examination 64% children were anaemic, 89% children presented with enlarged spleen, 74% had liver enlargement. None of the cases showed features of severe malaria.

Anaemia – haemoglobin of 8–10 g %–41% cases, and 6–8g % – 28.2% cases. There is no uniform variation in the degree of anaemia.

Total cell count – 4000 to 11,000 – 76%. The total white cell count usually remained within the range of normal in un complicated malarial infection. Mild increase is noted in severe forms.

Platelet count :< 1.5/cubic millimetre – 79.4%. The platelet count decreases in acute malaria but does not lead to severe thrombocytopenia except in profound cases.

Study Series Cases	Total Cases	Examined Positive	Percentage %
Jelinek T et al37(1999)	231	69	29.8
Palmer CJ et al38(2003)	216	43	20
Misra MN et al 39 (2007)	400	90	22.5
Malik S et al40 (2004)	124	59	47.5
Present study(2013)	160	32	20

Table above. 21: Peripheral blood smear positivity in suspected malaria cases

Compare rapid diagnostic test HRP2/PLDH with the peripheral blood smear examination.

Rapid diagnostic test using HRP 2/PLDH detected 37 cases to be positive for Plasmodium species, by the peripheral smear only 32 cases were detected. Seven cases of Plasmodium vivax detected by kit were not

detected by PBS. This can be explained by the fact that nowadays practising physicians in the name of presumptive treatment give unjudicious use of antimalarials as well as inadequate dosing. The LDH enzyme produced only by viable organisms and hence negative. Another reason for the discrepancy can be because of low levels of enzyme produced by parasite in the early stage of infection. It can also be due to the kit unable to detect the low levels of enzyme.

Another discrepancy was two cases detected by peripheral blood smear missed by rapid diagnostic tests. This can be explained by the fact that since one of the two are Plasmodium falciparum it could have been sequestered inside the organs and hence the blood did not contain the organism. One case was Plasmodium vivax this could've been because the organism was damaged during the process are there were other cross-reactive antibodies producing false-positive result in the rapid diagnostic test.

Table 22: Comparison results PBS Study and Hrp2/pLDH Test in different studies.

Study series	Percentage of positivity	
	PBS Study	Hrp2/pLDH Test
Carol J. Palmer et al41 (1998)	48%	45%
T. Jelinik T et al37 (1999)	29.8%	24.2%
Jamshaid Iqbal et al42 (2002)	36.1%	30.6%
Palmer CJ et al38 (2003)	20%	19%
Jamshaid Iqbal et al43 (2003)	42%	32%
Chayani N et al31 (2004)	52.5%	50.8%
Present study (2013)	20%	23.1%

In comparison of peripheral blood smear and rapid diagnostic test our study showed 20% in smear and 23.1% in the card to be positive. These values correlated well with Palmer CJ et al done on 2003 and Jelinek T et al in the year 1999. The others had a higher positive percentage as compared to our trial.

Table: Sensitivity and specificity of hrp2/ pLDH test for Pl.falciparum

Study series	Sensitivity	Specificity
Palmer CJ et al41 (1998)	88%	99%
Jelinik T et al37 (1999)	88.5%	99.4%
Jamshaid Iqbal et al42 (2002)	87%	99%
Chayani N et al31 (2004)	88.4%	99%
Present study (2013)	91.3%	96.3%

Table 24: Sensitivity and specificity of Hrp2/ pLDH test for Pl.vivax

Study series	Sensitivity	Specificity
Carol J. Palmer et al41 (1998)	94%	100%
Jelinik T et al37 (1999)	61.5%	100%
Jamshaid Iqbal et al41 (2002)	79%	97%
Chayani N et al31 (2004)	96.8%	100%
Present study (2013)	100%	98.7%

Sensitivity was around 91.3% to 100% and specificity of 96.3% to 98.7%. This was in comparison to the gold standard peripheral smear. The results showed positive correlation with Palmer CJ et al

Table 25: Positive predictive value and Negative predictive value of hrp2/pLDH test for Pl.falciparum malaria

Study series	PPV	NPV
Palmer CJ et al41 (1998)	88%	99%
Jelinik T et al37 (1999)	97.9%	96.7%
Jamshaid Iqbal et al42 (2002) A	94%	99%
Jamshaid Iqbal et al43 (2003)	89-97%	96-98%
Chayani N et al31 (2004)	92%	98.5%
Present study (2013)	80.8%	98.5%

Positive predictive value of our tests is 98.5% – 100%. It was in comparison peripheral blood smear. The results were similar to Palmer CJ et al Positive predictive value of study was 80.8% to 81.8%. The negative predictive value was around and Jelinek et al.

Table 26: Positive predictive value and Negative predictive value of hrp2/pLDH test for Pl.vivax malaria

Study series	**PPV**	**NPV**
Palmer CJ et al41 (1998)	100%	96%
Jelinik T et al37 (1999)	100%	97.8%
Jamshaid Iqbal et al42 (2002)	91%	93%
Jamshaid Iqbal et al43 (2003)	88-95%	90-93%
Chayani N et al31 (2004)	100%	97.8%
Present study (2013)	81.8%	100%

CONCLUSION

Peripheral blood smear examination for the diagnosis of malaria is a time-tested accurate investigation. Till now it is considered as the gold standard in the identification of malaria. The reasons for this reputation is, it is very cheap, all the organisms can be identified, the degree of parasitaemia can be found with high sensitivity. The disadvantage of the test is it require skilled technician and is time-consuming.

In the study we compact the rapid diagnostic test with the peripheral blood smear examination and identified that is almost similar inefficacy to it. Sensitivity of 91.3% and 100% specificity 96.3% and 98.7% for Plasmodium falciparum, Plasmodium vivax compared to peripheral smear examination.

An ideal test should be simple, rapid, specific, sensitive not requiring special equipments and requiring less technical skills. The rapid diagnostic test is all the above characters making it an ideal test in malaria diagnosis.

Here quality of RDT is on par with the PBS but the cost of the test kit is high limiting the use on a wide scale. On the short-term basis though it appears costly the burden of the disease due to resistant organisms arising as a result of our personal use of drugs seems to be more costly in the long run. Hence RDT helps malaria control on a long-term basis making accurate diagnosis and accurate treatment.

SUMMARY

- The study was conducted in Institute of social paediatrics on one stage children attending the hospital. Its aim is to identify the role of immune chromatographic antigen detection test in diagnosis of malaria.

- Out of the 160 children, 39 children were positive for malaria by any of the two methods either RDT or peripheral blood smear

- the symptomatology of these patients with malaria had fever universally (100%), followed by chills and rigours (51.2%), headache (38.5%), abdominal pain (35.9%).

- The signs commonly observed in this set of patients with malaria was pallor 64%, splenomegaly 89.7%, hepatomegaly 74.3%.

- Malaria positive by the card test – 32 cases (20%), Malaria positive by peripheral blood smear – 37 cases (23.1%).

- The Plasmodium vivax positivity in peripheral blood smear were 23 and Plasmodium falciparum was nine cases. The total positive for malaria was 32 cases.

- The Plasmodium vivax positive in rapid diagnostic test was 26 and Plasmodium falciparum was 11 cases. The total positive cases were 37.

- The sensitivity of rapid diagnostic test was 93.8% and a specificity of the RDT was 93.8%. These values are correlated compared with the gold standard test peripheral blood smear.

- Species-specific sensitivity of smear are Plasmodium falciparum sensitivity of 91% and specificity of 96%, Plasmodium vivax showing a sensitivity of 100% and specificity of 98.7%.

- Positive predictive value of the rapid diagnostic test using the HRP 2/PLDH showed falciparum to be 80.8% and vivax has 81.8%. The negative predictive value of Plasmodium falciparum was 98.5% and the same for Plasmodium vivax was 100%.

- The rapid diagnostic test was found to be comparable with and reliable with the peripheral blood smear. This test can be used in areas where peripheral blood smear cannot be done. The main drawback of the test is the high cost of the test and technically it is difficult to identify the disease severity using their rapid diagnostic test.

BIBLIOGRAPHY

1. Yogesh Jain. Cerebral and other types of severe malaria. In: Medical emergencies in children, 4th edition, Eds. Meherban Singh. New Delhi, Sagar publications, 2007; 308-317.

2. Crawley J, Chu C, Mtove G, Nosten F, Malaria in children. Lancet 2010;375:1468-81.

3. WHO: World Malaria Report. 2009: Geneva.

4. WHO: Malaria country profile, India 1995-2007.

5. Woodrow C.J, Repeiro I, Krishna S. Recent development in the management of Malaria, Indian J Pediatr 1999; 66: 103-109.

6. Kundu R, Ganguly N, Gosh T K, Chaudury P, Shah R C. Management of Malaria in Children: Update 2008 Infectious Diseases Chapter, Indian Academy Of Pediatrics; Indian Pediatrics; Volume 45__September 17, 2008;731-735.

7. Malaria rapid diagnostic performance. Results of WHO product testing of malaria RDT's: Round 2: 2009.

8. Chatterjee KD, Parasitology (Protozoology and Helminthology) In Relation To Clinical Medicine.12thEd. Kolkata, India: Chatterjee Medical Publishers;1980;71-80.

9. Wernsdorfer WH, Mc Gregor SI, Malaria; Principles and practice of Malariology. Edinburg; Churchill Livingstone; 1998; 782-813.

10. Park J.E, Park K. Epidemiology of communicable diseases. In: Park's Textbook Of Preventive And Social Medicine, 19th Edn. Park J.E, Park K. Jabalpur, M/s Banarsidas Bhanot publishers, 2007; 209-20.

11. Ghai OP, Infections And Infestations,Malaria. In: Ghai Essential Pediatrics, 7th Edn. Ghai OP, Paul VK ,Bagga A , Delhi, Dr. O.P Ghai, CBS publishers & distributors;2009; p227-237.

12. Nicholas J. White, Joel G.Breman. Malaria and Babesiosis: Diseases caused by red blood cell parasites. In: Harrison's Principles of Internal Medicine. 16th Edn. Eds. Braunwald, Fauci, Kasper, Houser, Longo. Unites States of America, the Mc Graw-Hill companies, Inc., 2005; p1221-1230.

13. Nicholas J. White. Malaria. In: Manson's tropical disease, 20th Edn. Eds Gordon Cook, London, Harcourt Pvt. Ltd., 2001; p1087- 1164.

14. D.J. Bradley, D.A. Warrell. Malaria In: Oxford textbook of medicine, 4th Edn. Eds. David A. Warrell, Timothy M. Cox, Joh D. Firth, New York, Oxford University Press Inc., 2003; p721- 748.

15. B. Anjaiah. Cerebral malaria. In: Clinical Pediatrics, 2nd Edn.. Hyderabad, Paras Medical Publishers, 2003: p175-178.

16. Houwen B. Blood film preparation and staining procedure, Clin Lab Med 2002; 22: 1-14.

17. Nandy A. National antimalarial drug policy and its implications in the malaria control in India. In: Ganguly N, Kundu R, Gosh T.K, Eds. Common MDR infections in children. Thyroid, Tuberculosis, Malaria. New Delhi: CBS publication, 2005: 197-207.

18. WHO. Diagnosis of Malaria in Management of Severe Malaria. A practical handbook 2nd Edn. Geneva: WHO, 2000; 46-8.

19. Anthony Moody. Rapid Diagnostic Test for Malaria parasites, Clina Microbiol Rev, Jan 2002; 15 (1): 66-78.

20. Baird J.K, Puranomo, T.R. Jones. Diagnosis of malaria in the field by florescence microscopy of QBC capillary tubes. Trans R Soc Trop Med Hyg, 1992; 86: 3-5.

21. Clendeman T.E, G.W. Long, J.K. Baird. QBC and Giemsa stained thick blood films: Diagnostic performance of laboratory technologists. Trans R Soc Trop Med Hyg, 1995; 86: 378.

22. Craig M, B.L. Sharp. Comparative evaluation of four techniques for the diagnosis of plasmodium infections. Trans R Soc Trop Med Hyg, 1997; 91: 279-282.

23. Gaye O, M. Diouf, S. Diallo. A comparison of thick films, QBC malaria, PCR and PATH falciparum malaria test strip in plasmodium falciparum diagnosis. Parasite, 1999; 6: 273-275.

24. Wongsrichanalai C, J. Pornsilapatip, V. Namsiriponpun, H.K. Webster, A.Luccini, P. Pansamdang et al. Acridine orange fluorescent microscopy and detection of malaria in populations with low density parasitemia. Am. J Trop Med Hyg, 1991; 44: 17-20.

25. Rock EP, K. Marsh, S.J. Saul, TE Wellems, D.W Taylor, W.L. Maloy, et al. Comparative analysis of plasmodium falciparum histidine rich proteins HRP-1, HRP-2 and HRP-3 in malaria diagnosis of diverse origin. Parasitology, 1987; 95: 209-227.

26. Shiff C.J, Premji Z, Minjas J.N. The manual ParaSight – F test. A new diagnostic tool for plasmodium falciparum infection. Trans R Soc Trop Med Hyg 1993; 87: 646-648.

27. Makler MT, Palmer C.J, Ageral. A review of practical techniques for diagnosis of malaria. Am. Trop Med Parasitol, 1998; 92: 419-433.

28. Makler M.T, J.M. Ries, J.A. Williams, J.E. Bancroft, R.C. Piper, B.L. Gibbins, et al. Parasite lactate dehydrogenase as an assay for plasmodium falciparum drug sensitivity. Am J Trop Med Hyg, 1993; 48: 739-741.

29. Kakkilaya BS. Rapid Diagnosis of Malaria.Lab Medicine. M.JOURNAL 2003 Aug;8(34):602-608

30. Jelinek T ,Kilian AHD , Henk M , et al. Parasite specific lactate dehydrogenase for the diagnosis of plasmodium falciparum infection in an endemic area in west Uganda .Trop Med Int Health 1996;1(2): 227-30.

31. Chayani N, B. Das, M. Sur, S. Bajoria. Comparison of parasite lactate dehydrogenase based immunochormatographic antigen detection assay (OptiMal) with microscopy for detection of malaria parasites. Indian J Med Microbiol 2004; 22 (2): 104-106.

32. Chiodini PL, Bowers K , Jorgensen P, et al. The heat stability of plasmodium lactate dehydrogenase – based and histidine rich protein based 2 based malaria rapid diagnostic tests .trans R Soc Trop Med Hyg ;2007;101:3317.

33. Krause P J,Jhon C C. Malaria (plasmodium) Nelson Textbook of pediatrics, Eds Kleigman R M, Behrman R E, Schor NF, Stanton B F.19th ed. Gurgaon, Elsevier publication: 2012; 1198-1207.

34. Price RN, Douglas NM, Anstey NM, New developments in plasmodium vivax malaria: severe disease and the rise of chloroquine resistance .CurrOpin Infect Dis 2009;22:430-435.

35. Mishra R.Pediatric malaria.in:Gupte S, Sobti PC (eds): Recent Advances in Pediatrics -18 Hot Topics .New Delhi :Jaypee 2009; 173-205.

36. Dowling M.A.C, Shute G.T. A comparative study of thick and thin blood films in the diagnosis of scanty malaria parasitemia. Bull WHO 1996; 34:p249-267.

37. T. Jelinek, M.P. Grobusch, S. Schwenke. Sensitivity and specificity of dipstick test for rapid diagnosis of malaria in non immune travelers.
J Clin Microbiol 1999; 37(3): 721-723.

38. Carol J. Palmer, J. Alfredo Bonilla, David A. Bruckner. Multicentre study to evaluate the OptiMal test for rapid diagnosis of malaria in US hospitals. J.Clin Microbiol 2003; 41(11): 5178-5182.

39. Mishra MN. Mishra RN, Immunochromatographic Methods in Malaria Diagnosos, MJAFI 2007; 63:127-129.

40. Malik S, Khan S, Das A et al. plasmodium lactate dehydrogenase assay to detect maarial parasites. Natl Med J India; 2004 sep-oct ; 17(5):237-9.

41. Carol J. Palmer, John F. Lindo, Winslow I. Evaluation of the OptiMal Test for rapid diagnosis of plasmodium vivax and plasmodium falciparum malaria. J. Clin Microbiol 1998; 36(1): 203-206.

42. Jamshaid Iqbal, Nabila Khalid, Parsotam R. Hira. Comparison of commercial assay with expert microscopy for confirmation of symptomatically diagnosed malaria. J Clin Microbiol 2002; 40(12): 4675-4678.

43. Jamshaid Iqbal, Arif Muneer, Nabila Khalid. Performance of the OptiMAL test for malaria diagnosis among suspected malaria patients at the rural health centers. Am J Trop Med Hyg, 2003; 68(5): 624-628.a

PROFORMA

ROLE OF IMMUNOCHROMATOGRAPHIC ANTIGEN DETECTION ASSAY IN THE EARLY DETECTION OF MALARIA

PATIENT NAME :

AGE :

SEX :

ADDRESS :

IP No. :

DOA&DOD :

CHIEF COMPLAINTS	YES	NO
1) FEVER		
2) CHILLS AND RIGORS		
3) HEADACHE		
4) SWEATING		

5) CONVULSION

6) ALTERED SENSORIUM

7) VOMITING

8) PAIN ABDOMEN

9) OTHERS

VITALS

1) HEART RATE

2) RESPIRATORY RATE

3) BLOOD PRESSURE

4) TEMPERATURE

ANTHROPOMETRY

1) WEIGHT

2) HEIGHT

3) WEIGHT FOR AGE

GENERAL EXAMINATION

1) PALLOR

2) ICTERUS

3) PETECHIAE/ PURPURA

SYSTEMIC EXAMINATION:

- P/A HEPATOMEGALY—IF YES SIZE/ CONSISTENCY

  SPLENOMEGALY – IF YES SIZE/ CONSISTENCY

  CVS RS CNS

  LABORATORY DATA

- CBC
- IMMUNOCHROMATOGRAPHIC TEST
- PERIPHERAL SMEAR

  ADDITIONAL TESTS AS REQUIRED

  1)WIDAL 2) URINE ROUTINE 3) MSAT 4) URINE C/S

  FINAL DIAGNOSIS:

KEY TO MASTER CHART

M	- Male
F	- Female
OP	- Outpatient
IP	- Inpatient
P	- Present
A	- Absent
PA	- Pain Abdomen
VO	- Vomiting
CO	- Convulsion
Wt	- Weight
Ht	- Height
Wt. for age	- Weight for age
HR	- Heart Rate
RR	- Respiratory rate
BP	- Blood Pressure
Temp.	- Temperature
Hb%	- Hemoglobin Percentage
TC	- Total cell count

DC - Differential count

N% - Neutrophil percentage

M% - Monocyte percentage114

L% - Lymphocyte percentage

Plt - Platelet

Pl.f - Plasmodium falciparum

Pl.v - Plasmodium vivax

F.malaria - Falciparum malaria

V.malaria - Vivax malaria

GPf - Gametocyte of Plasmodium falciparum

RPf - Ringform of of Plasmodium falciparum

LTPv - Late Trophozoite of Plasmodium vivax

SPv - Schizont of Plasmodium vivax

RPv - Ringform of Plasmodium vivax

V.Encephalitis – Viral Encephalitis

+ - Positive

- - Negative

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"THE ROLE OF IMMUNOCHROMATOGRAPHIC ANTIGEN DETECTION ASSAY IN THE EARLY DIAGNOSIS OF MALARIA"

Dissertation submitted to

THE TAMIL NADU DR. M. G. R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations for the award of degree of

M.D DEGREE (PEDIATRICS) BRANCH VII

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PAGE: 1 OF 122

Text-Only Report

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Role of Immunochromatographic antigen detection assay in the early Diagnosis of Malaria.

Principal Investigator : Dr. R Anand

Designation : PG in MD (Paediatrics)

Department : Department of Paediatrics
Government Stanley Medical College,
Chennai-01

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 05.08.2014 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY,
IEC, SMC, CHENNAI

சுய ஒப்புதல் படிவம்

மலேரியா காய்ச்சல் அறிகுறிகள் உள்ள குழந்தைகளுக்கு எளிதல் கண்டுபிடிக்கக் கூடிய இரத்த சோதனை முறை பற்றி ஆராய்தல்

ஆராய்ச்சி நிலையம் : குழந்தைகள் சமூக நல மருத்துவப்பிரிவு
அரசு ஸ்டான்லி மருத்துவமனை,
சென்னை - 600 001.

பங்கு பெறும் நோயாளியின் பெயர் : வயது

பங்கு பெறும் நோயாளியின் எண் : பாலினம்: ஆண் ☐ பெண் ☐

நோயாளியின் விலாசம் :

நோயாளி இதனை (✓) குறிக்கவும் :

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் என் குழந்தையை தன்னிச்சையாகதான் பங்கேற்க அனுமதிக்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் என் குழந்தையை இவ்வாய்வில் இருந்து விலக்கிக் கொள்ளலாம் என்று அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவும் மேலும் இதை சார்ந்த ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என் குழந்தையின் மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். என் குழந்தையை ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். என் குழந்தைக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடத்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதி அளிக்கிறேன். என் குழந்தையின் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்க்குறி தென்பட்டாலோ உடனே அதனை மருத்துவ அணிக்கு தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

இந்த ஆய்வில் என் குழந்தைக்கு இரத்தம், சிறுநீர், எக்ஸ்ரே, ஸ்கேன் உட்பட அனைத்து பரிசோதனைகளையும் செய்து கொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி .....

கட்டை விரல் (இந்த படிவம் படித்து காட்டப்பட்டு புரிந்து கைரேகை அளிக்கிறேன்)

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம் .....தேதி .....

ஆய்வாளரின் பெயர் .....

தகவல் படிவம்

மலேரியா காய்ச்சல் அறிகுறிகள் உள்ள குழந்தைகளுக்கு எளிதல் கண்டுபிடிக்கக் கூடிய இரத்த சோதனை முறை பற்றி ஆராய்தல்

ஆராய்ச்சியின் நோக்கமும், பயன்களும் :

மலேரியா காய்ச்சல் உள்ள அறிகுறிகளோடு வரக்கூடிய குழந்தைகளுக்கு, வழக்கமாக பரிசோதனை செய்யக்கூடிய இரத்தப்பரிசோதனைகளோடு புதிய முறையில் அதிவேகமாக கண்டுபிடிக்கக்கூடிய இரத்தப் பரிசோதனையை சேர்த்து செய்து, பரிசோதனையின் பலினமையை கண்டறிதல் அதன் மூலம் வியாதியை சரி உபாக விரைவில் கண்டுபிடித்த

ஆய்வு நடைமுறைகள் :

சிகிச்சை அளிப்பதற்கு ஏற்பாடு செய்தல் இவ்வாராய்ச்சியின் நோக்கமாகும். உள்நோயாளிகளாக அல்லது வெளி நோயாளியாக உள்ள மலேரிய காய்ச்சல் அறிகுறிகள் உள்ள குழந்தைகள் இந்த ஆராய்ச்சியில் சேர்த்துக் கொள்ளப்படுவார்கள்.

அந்தரங்க தன்மை :

உங்கள் குழந்தையின் மருத்துவ பதிவேடுகள் மிகவும் அந்தரங்கமாக வைத்துக் கொள்ளப்படும் மற்றும் பிற மருத்துவர்கள் / விஞ்ஞானிகள் / இந்த ஆய்வின் தனிக்கையாளர்கள் அல்லது ஆராய்ச்சி ஆதரவாளர்களின் பிரதி நிதிகள் ஆகியோரிடம் அவை வெளிப்படுத்தப்படும். இந்த ஆய்வின் முடிவுகள் அறிவியல் பத்திரிக்கைகளில் பரிசுரிக்கப்படலாம். ஆனால் பெயரை வெளியிடுவதன் மூலம் நோயாளியின் அடையாளம் காட்டப்பட மாட்டார்கள்.

ஆய்வில் உங்கள் பங்கேற்பு மற்றும் உங்கள் உரிமைகள் :

இந்த ஆய்வில் உங்கள் குழந்தைகளின் பங்கேற்பு முழுவதும் உங்களுடைய விருப்பத்தை சார்ந்தது. இதில் நீங்கள் பங்கேற்கவோ, மறுக்கவோ, பாதியில் வெளியேரிடவோ அல்லது குறிப்பிட்ட கேள்விகளுக்கு பதிலளிக்க மறுக்கவோ உங்களுக்கு முழு உரிமை உண்டு எப்படி இருந்தாலும் உங்கள் குழந்தையின் உடல் நிலைக்கேற்ப உங்கள் குழந்தைக்கு பொருத்தமான சிகிச்சை அளிக்கப்படும் தாங்கள் இது குறித்து வேறு விபரங்கள் தெரிந்து கொள்ள விரும்பினால் எங்களிடம் கேட்டுத் தெரிந்து கொள்ளலாம்.

மேலும் விபரங்கள் அறிய கீழ்க்கண்ட நபரை அணுகவும் :
மரு.இரா.ஆனந்த்
பட்டமேற்படிப்பு மாணவர்
குழந்தைகள் நல மருத்துவம்
அரசு ஸ்டான்லி மருத்துவ கல்லூரி, சென்னை
தொலைப்பேசி எண்.9003835452

MASTER CHART

SL. NO.	OP/IP NO.	AGE (YEARS)	SEX	COMPLAINTS							ANTHROPOMETRY	GPF			VITALS	HAPATOMEGALY		SPLEENOMEGALY		HB@	TC	DC			PLATELETS	HRP2/PLDH		PERIPHERAL SMEAR		Final Daignosis
				FEVER	CHILLS & RIGORS	SWEATING	HEADACHE	PAIN ABDOMEN	ALTERED SENSORIUM	OTHERS		PALLOR	ICTERUS	PETECHIAE OR PURPURA		SIZE IN CMS	CONSISTENCY	SIZE IN CMS	CONSISTENCY			N%	L%	M%		Pl.V	Pl.F	Thick	Thin	
1	1451550	4	F	P	P	P	A	A	A	A	74.59	P	A	A	S	2	Soft	2.5	soft	8.70	5200	64	34	2	1	+	-		PL.V	vivax.mal
2	1451555	7	F	P	P	A	A	A	A	VO	90.5	A	A	A	S	2.5	Soft	2	soft	10.00	9200	54	44	2	0.8	-	-	-	-	viral fever
3	145435	8	M	P	P	A	A	P	A	A	74.5	P	A	A	S	2	Soft	1.5	soft	9.00	8700	42	54	4	0.4	-	-	-	-	viral fever
4	145566	6	M	P	P	A	A	A	A	VO	94.5	P	A	A	S	1	firm	1.5	firm	9.80	2670	50	48	2	2	-	-	-	-	Enteric Fever
5	506856	12	M	P	P	A	P	A	A	A	90.2	P	A	A	S	1	Soft	2	soft	7.20	6700	58	40	2	1.2	-	+	PL.F	PL.F	Fal.malaria
6	506960	12	F	P	A	A	P	A	A	A	75.9	P	A	A	S	2.5	-	A	-	8.60	1200	45	50	5	0.3	-		-	-	viral fever
7	145794	10	M	P	A	A	P	A	A	A	86.5	A	A	A	S	A	firm	3	firm	11.20	10200	66	27	7	3.4	-	-	-	-	Enteric Fever
8	1455293	8	F	P	A	A	P	A	A	VO	78.5	A	A	A	S	2	Soft	1	soft	11.90	3900	62	32	6	1.5	-	-	-	-	viral fever
9	1455202	10	F	P	P	A	P	A	A	A	86.1	P	A	A	S	2	Soft	3	soft	9.20	9600	56	44	0	0.96	+	-	-	pl.v	V.Malaria
10	1451696	11	F	P	P	A	P	A	A	A	95.7	P	A	A	S	3	Soft	2	soft	10.80	7600	46	50	4	3.2	-	-	-	-	viral fever
11	1451683	9	F	P	P	A	A	P	A	A	86.3	A	A	A	S	1	-	A	-	11.20	4200	44	51	5	1.08	-	-	-	-	Enteric Fever
12	1451643	8	M	P	A	A	P	P	A	A	74.5	A	A	A	S	1.5	Soft	1	soft	12.40	4800	28	70	2	1.4	-	-	-	-	Viral fever
13	1451788	4	M	P	A	A	A	A	A	VO	84.5	P	A	A	S	2	Soft	3	soft	8.10	13000	64	28	8	0.76	-	-	-	-	Enteric Fever
14	506797	12	F	P	P	P	P	A	A	VA	80.2	P	A	A	S	2	Soft	2.5	soft	6.20	7000	56	42	2	3.3	-	+	pl.f	pl.f	Fal.malaria
15	1451348	8	M	P	P	A	A	A	A	A	78.4	A	A	A	S	1	Soft	2	soft	12.40	11200	46	47	6	1.03	-	-	-	-	Viral fever
16	1451034	9	M	P	A	A	P	A	A	A	92.8	P	A	A	S	A	-	1	soft	9.60	3500	44	51	5	1.04	-	-	-	-	Enteric Fever
17	1452110	12	M	P	P	A	P	A	A	A	95.4	A	A	A	S	2	Soft	A	-	12.60	6700	62	33	5	1.9	-	-	-	-	Viral fever
18	1451968	9	M	P	A	A	P	P	A	A	86.8		A	A	S	3	Soft	1.5	firm	10.00	9600	68	30	2	1.3	-	-	-	-	Enteric Fever
19	1451173	6	M	P	P	A	A	P	A	A	80.2		A	A	S	2	Soft	A	-	9.6	11200	46	47	6	3.3	-	-	-	-	viral fever
20	1451531	7	M	P	P	A	A	P	A	A	81.8		A	A	S	1	Soft	2.5	soft	10.6	4500	60	36	4	1.8	-	+	PL.F	pl.f	Fal.malaria
21	1451559	10	M	P	A	A	P	A	A	A	76.9		A	A	S	1.5	Soft	2	soft	13	7000	56	42	2	3.3	-	-	-	-	Enteric Fever
22	1451584	6	M	P	P	A	A	A	A	A	90.5		A	A	S	A	-	3	soft	12	8700	62	32	6	1.5	-	-	-	-	Viral fever
23	1451630	7	M	P	A	P	A	P	A	A	81.8		A	A	S	1.5	Soft	2	soft	13	9500	70	28	2	1.5	-	-	-	-	viral fever
24	1451680	4	F	P	A	A	P	A	A	VO	85.2		A	A	S	2	Soft	A	-	6.5	12300	64	34	2	3.1	-	-	-	-	Enteric Fever
25	1451663	7	F	P	A	A	P	A	A	A	77.2		A	A	S	1.5	Soft	2	soft	11.5	8700	62	32	6	1.5	-	-	-	-	Viral fever
26	507227	12	M	P	P	A	A	A	A	A	81.2		A	A	S	A	-	3	soft	9	8600	58	40	2	1.2	+	-	-	pl.v	vivax.mal
27	5072176	10	M	P	A	A	P	A	A	A	76.2		A	A	S	2	Soft	1	soft	8.3	7000	56	42	2	3.3	-	-	-	-	Viral fever
28	1451850	6	M	P	A	A	P	A	A	A	80.2		A	A	S	3	Soft	2	soft	7.8	10000	70	28	2	1.5	-	-	-	-	Enteric Fever
29	1452067	11	M	P	P	A	A	A	A	A	85.6		A	A	S	2	Soft	2	soft	8.7	6500	62	32	6	1.5	-	-	-	-	Viral fever
30	145208	12	F	P	P	P	A	A	A	VO	82.5		A	A	S	3	Soft	1	soft	12.4	7300	58	40	2	2.2	-	-	-	-	Viral fever
31	1451189	6	M	P	P	A	P	A	A	A	80.2		A	A	S	A	-	2	soft	9.8	9200	64	34	2	3.1	-	-	-	-	Viral fever
32	507225	9	F	P	P	A	P	A	A	VO	92.5		A	A	S	2	Soft	2	soft	9.9	7600	73	21	5	1.4	-	+	PL.F	PL.F	Fal.malaria
33	507219	12	F	P	P	A	P	A	A	VO	76.5		A	A	S	1	Soft	2	soft	11	7000	56	42	2	3.3	-	-	-	-	Viral fever
34	1452138	7	M	P	A	A	P	A	A	A	86.4		A	A	S	2	Soft	2	soft	10	11300	70	28	2	1.5	-	-	-	-	viral fever
35	14520380	5	M	P	P	A	A	A	A	VO	84.5		A	A	S	3	Soft	1	soft	9.5	12100	62	32	6	1.5	-	-	-	-	viral fever
36	1452064	6	M	P	P	A	P	A	A	A	80.2		A	A	S	2	Soft	1	soft	10	7600	58	40	2	2.2	-	-	-	-	Enteric Fever
37	1451642	12	F	P	A	A	P	A	A	A	95.2		A	A	S	A	-	1	soft	9.3	3300	88	40	2	0.5	-	+	GPF	GPF	Fal.malaria
38	1451645	4	M	P	A	A	A	P	A	VO	74.5		A	A	S	3	Soft	2	soft	7.5	7000	56	42	2	3.3	-	-	-	-	viral fever
39	1451660	12	F	P	A	A	P	A	A	A	76.9		A	A	S	3	Soft	2	firm	10	5400	80	18	2	1	-	-	-	-	Enteric Fever
40	1451715	11	F	P	P	A	P	P	A	A	94.6		A	A	S	2	Soft	1	soft	12	3600	62	32	6	1.5	-	-	-	-	Viral fever
41	1451775	10	M	P	P	A	P	A	A	A	86.5		A	A	S	A	-	A	-	9.5	10900	64	34	2	3.1	-	-	-	-	viral fever
42	507027	12	M	P	P	A	A	A	A	VO	81.2		A	A	S	2	Soft	3	soft	8	9200	40	54	6	2.5	+	-	-	PLV	vivax.mal
43	1452382	5	F	P	P	A	A	A	A	VO	82.5		A	A	S	2	Soft	2	soft	10	7000	56	42	2	3.3	-	-	-	-	Enteric Fever
44	1452418	12	F	P	P	A	A	A	A	A	76.2		A	A	S	2	Soft	A	-	11	11200	62	32	6	1.5	-	-	-	-	Viral fever
45	507016	3	M	P	A	A	P	A	A	VO	78.6		A	A	S	3	Soft	1	soft	12	5900	80	18	2	1	-	-	-	-	Viral fever
46	507086	8	F	P	P	A	A	A	A	VO	78.4		A	A	S	2	Soft	A	-	9	9900	64	34	2	3.1	-	-	-	-	viral fever
47	1452554	12	M	P	P	A	P	A	A	A	75.5		A	A	S	2	Soft	1	soft	12	8400	70	28	2	1.5	-	-	-	-	Enteric Fever
48	507033	10	M	P	A	A	P	P	A	A	86.5		A	A	S	1	Soft	2	soft	7	3300	48	43	9	0.7	+	-	-	PV	vivax.mal
49	1452565	4	F	P	A	A	A	P	A	VO	74.2		A	A	S	4	Soft	2	soft	10	7000	56	42	2	3.3	-	-	-	-	Viral Fever
50	507004	7	F	P	A	A	A	A	A	A	85.2		A	A	S	A	-	1	soft	7	10300	62	32	6	1.5	-	-	-	-	Viral Fever
51	1451850	12	M	P	A	A	A	A	A	A	75.2		A	A	S	2	Soft	2	soft	12	13500	58	40	2	2.2	-	-	-	-	Enteric Fever
52	1452587	6	F	P	A	A	A	A	A	A	80.2		A	A	S	3	Soft	A	-	10	4700	64	34	2	3.1	-	-	-	-	Viral Fever

SL. NO.	OP/IP NO.	AGE (YEARS)	SEX	COMPLAINTS							ANTHROPOMETRY	GPF			VITALS	HAPATOMEGALY		SPLEENOMEGALY		HB@	TC	DC			PLATELETS	HRP2/PLDH		PERIPHERAL SMEAR		Final Daignosis
				FEVER	CHILLS & RIGORS	SWEATING	HEADACHE	PAIN ABDOMEN	ALTERED SENSORIUM	OTHERS		PALLOR	ICTERUS	PETECHIAE OR PURPURA		SIZE IN CMS	CONSISTENCY	SIZE IN CMS	CONSISTENCY			N%	L%	M%		Pl.V	Pl.F	Thick	Thin	
53	1452626	12	M	P	A	A	A	A	A	A	95.2		A	A	S	1	Soft	1	soft	9.9	10300	70	28	2	1.5	-	-	-	-	Enteric Fever
54	1452625	12	M	P	P	A	A	A	A	A	76.5		A	A	S	1	Soft	1	soft	8	4900	82	11	7	1.4	-	+	PL.F	PL.F	Fal.malaria
55	507077	6	F	P	A	A	A	A	A	A	78.2		A	A	S	2	Soft	A	-	10	11300	62	32	6	1.5	-	-	-	-	Viral Fever
56	1452635	9	F	P	A	A	A	A	A	A	89.26		A	A	S	1	Soft	A	-	12	5500	43	51	6	1.5	-	-	-	-	Enteric Fever
57	1452638	4	M	P	A	A	A	A	A	A	78.26		A	A	S	1	Soft	1	soft	11	7000	56	42	2	3.3	-	-	-	-	Viral Fever
58	507179	7	F	P	A	A	P	A	A	A	84.2		A	A	S	3	Soft	2	soft	9	4500	58	40	2	2.2	-	-	-	-	viral fever
59	507036	6	M	P	A	A	A	A	A	A	82.6		A	A	S	3	Soft	2	firm	10	9900	43	51	6	1.5	-	-	-	-	Enteric Fever
60	1452888	8	F	P	A	A	A	A	A	A	80.6		A	A	S	A	-	2	soft	10	10500	70	28	2	1.5	-	-	-	-	Viral Fever
61	1452594	12	M	P	P	A	A	A	A	A	95.2		A	A	S	A	-	1	soft	9	4300	62	32	6	1.5	-	-	-	-	Viral Fever
62	1452878	9	M	P	A	A	P	A	A	A	89.2		A	A	S	2	Soft	3	soft	11	6700	32	64	4	1.2	+	-	-	PV	vivax.mal
63	507080	12	M	P	A	A	A	A	A	A	95.6		A	A	S	2	Soft	2	soft	8	7000	56	42	2	3.3	-	-	-	-	Viral fever
64	1459264	6	F	P	A	A	P	A	A	A	82.2		A	A	S	A	-	1	firm	12	6500	64	34	2	3.1	-	-	-	-	Viral Fever
65	1453003	8	M	P	A	A	A	A	A	A	82.4		A	A	S	2	Soft	1	soft	10	7700	43	51	6	1.5	-	-	-	-	Enteric Fever
66	1453111	7	F	P	P	A	A	P	A	A	81.2		A	A	S	A	-	1	soft	9	8800	62	32	6	1.5	-	-	-	-	Viral Fever
67	507096	11	F	P	A	A	A	A	A	A	75.4		A	A	S	A	-	1	soft	8	11300	58	40	2	2.2	-	-	-	-	Enteric Fever
68	1453249	12	M	P	P	P	A	A	A	A	74.4		A	A	S	2	Soft	3	firm	10	6900	32	64	4	1.06	+	-	-	PV	vivax.mal
69	1453399	8	M	P	A	A	A	A	A	A	90.5		A	A	S	A	-	1	soft	8	6500	64	34	2	3.1	-	-	-	-	Viral fever
70	1453436	11	M	P	A	A	A	A	A	A	70.4		A	A	S	2	Soft	1	soft	11	7000	56	42	2	3.3	-	-	-	-	Viral Fever
71	1453478	7	M	P	A	A	P	A	A	A	84.2		A	A	S	3	Soft	1	soft	9.5	8300	62	32	6	1.5	-	-	-	-	Viral Fever
72	1452934	8	F	P	A	A	A	A	A	A	82.6		A	A	S	2	Soft	2	soft	8.4	4900	62	32	6	1.5	-	-	-	-	Viral Fever
73	1453602	7	M	P	A	A	A	A	A	A	84.2		A	A	S	3	Soft	1	soft	10	7900	70	28	2	1.5	-	-	-	-	Enteric Fever
74	1455630	10	F	P	P	A	A	A	A	A	78.4		A	A	S	2	Soft	2	soft	10.6	7000	56	42	2	3.3	-	-	-	-	Viral Fever
75	507661	10	M	P	A	A	P	P	A	A	80		A	A	S	3	Soft	3	soft	11.2	9700	60	36	4	1.16	-	+	PL.F	PL.F	Fal Malaria
76	507313	9	F	P	A	A	A	A	A	A	82.1		A	A	S	2	Soft	A	-	9.9	9900	62	32	6	1.5	-	-	-	-	Viral Fever
77	1455253	9	M	P	A	A	A	A	A	A	82.5		A	A	S	3	Soft	1	soft	10	8400	64	34	2	3.1	-	-	-	-	Enteric Fever
78	1453438	6	F	P	A	A	A	A	A	A	83.4		A	A	S	2	Soft	2	soft	11	11300	70	28	2	1.5	-	-	-	-	Viral Fever
79	1455808	8	M	P	A	A	A	A	A	A	82.6		A	A	S	1	Soft	2	soft	11	7000	56	42	2	3.3	-	-	-	-	Viral Fever
80	507271	10	M	P	A	P	A	A	A	A	74.6		A	A	S	2	Soft	A	-	10	10900	62	32	6	1.5	-	-	-	-	Viral Fever
81	1453825	8	M	P	P	A	A	P	A	A	85.2		A	A	S	2	Soft	2	soft	9	6900	40	56	4	1.35	-	+	PL.F	PL.F	Fal Malaria
82	507799	9	F	P	A	A	A	A	A	A	92.5		A	A	S	3	Soft	1	soft	11	7000	56	42	2	3.3	-	-	-	-	Viral Fever
83	1453862	12	F	P	A	A	A	A	A	A	74.4		A	A	S	3	Soft	A	-	10	7500	58	40	2	2.2	-	-	-	-	Viral Fever
84	507157	8	M	P	A	A	A	A	A	A	78.4		A	A	S	A	-	A	firm	11	8900	70	28	2	1.5	-	-	-	-	Viral Fever
85	1451209	10	M	P	P	A	P	A	A	A	76.9		A	A	S	2	Soft	2	soft	10	6700	36	58	4	1.3	+	-	-	PV	vivax.mal
86	1455864	6	F	P	A	A	A	A	A	A	83.2		A	A	S	A	-	A	-	7	7000	56	42	2	3.3	-	-	-	-	Viral fever
87	507064	10	F	P	A	A	A	A	A	A	78.4		A	A	S	3	Soft	1	soft	11	5500	62	32	6	1.5	-	-	-	-	Viral Fever
88	1453876	4	M	P	A	A	A	A	A	A	71.2		A	A	S	2	Soft	2	soft	11	8800	64	34	2	3.1	-	-	-	-	Enteric Fever
89	1453859	8	M	P	P	P	A	A	A	A	82.6		A	A	S	2	Soft	3	soft	10	9650	42	56	2	1.06	+	-	-	PV	vivax.mal
90	1453718	9	F	P	A	A	A	A	A	A	75.2		A	A	S	2	Soft	3	soft	10	7000	56	42	2	3.3	-	-	-	-	Viral Fever
91	1453995	10	M	P	A	A	A	A	A	A	73.5		A	A	S	3	Soft	1	firm	10	9400	43	51	6	1.5	-	-	-	-	Viral fever
92	1454036	10	M	P	P	A	A	A	A	A	76.9		A	A	S	1	Soft	2	soft	7.2	8300	62	32	6	1.5	-	-	-	-	Viral Fever
93	1454043	8	M	P	A	A	P	P	A	A	78.4		A	A	S	A	-	1	soft	9.5	9800	42	54	4	0.7	+	-	-	PV	vivax.mal
94	1454088	9	M	P	A	A	A	A	A	A	82.1		A	A	S	3	Soft	1	soft	8.4	7700	73	20	7	2.2	-	-	-	-	Viral Fever
95	507363	12	M	P	P	P	A	A	A	VO	94.5		A	A	S	2	Soft	2	soft	10	4200	28	64	8	1.03	+	-	-	PV	vivax.mal
96	1455862	10	F	P	A	A	A	A	A	A	80		A	A	S	A	-	1	soft	10.4	7000	56	42	2	3.3	-	-	-	-	Enteric Fever
97	1454138	8	F	P	A	A	A	A	A	A	86.5		A	A	S	2	Soft	2	soft	11.4	9500	62	32	6	1.5	-	-	-	-	Viral fever
98	1454153	7	M	P	A	A	A	A	A	A	81.5		A	A	S	1	Soft	3	firm	7.4	5900	70	28	2	1.5	-	-	-	-	Viral Fever
99	1454286	12	M	P	P	P	A	A	A	A	74.2		A	A	S	1	Soft	A	-	8.4	6400	28	64	8	0.7	+	-	-	PV	vivax.mal
100	501373	9	F	P	P	A	A	P	A	A	92.8		A	A	S	1	Soft	2	soft	10.4	6500	64	34	2	3.1	-	+	PL.F	PL.F	Fal Malaria
101	1454296	8	M	P	A	A	A	A	A	A	78.2		A	A	S	1	Soft	1.5	soft	11.3	7000	56	42	2	3.3	+	-	-	PV	vivax.mal
102	507338	7	M	P	A	A	A	A	A	A	85.6		A	A	S	A	-	2	firm	12	6800	58	40	2	2.2	-	-	-	-	Enteric Fever
103	1454368	10	M	P	A	A	A	A	A	A	74.6		A	A	S	1.5	Soft	2	soft	7	5500	43	51	6	1.5	-	-	-	-	Viral Fever
104	1454322	11	M	P	A	A	A	A	A	A	95.4		A	A	S	A	-	1	soft	10	12300	62	32	6	1.5	-	-	-	-	Viral Fever
105	507330	10	M	P	A	A	P	A	A	A	86.5		A	A	S	1.5	Soft	1	soft	9.5	7000	56	42	2	3.3	-	-	-	-	Viral Fever
106	1454570	12	F	P	A	A	A	A	A	A	82.5		A	A	S	A	-	2	soft	9.5	11300	64	34	2	3.1	-	-	-	-	Viral Fever
107	1454552	9	M	P	A	A	A	A	A	A	86.3		A	A	S	2.5	Soft	1	soft	8.4	10000	70	28	2	1.5	-	-	-	-	Enteric Fever

SL. NO.	OP/IP NO.	AGE (YEARS)	SEX	COMPLAINTS							ANTHROPOMETRY	GPF			VITALS	HAPATOMEGALY		SPLEENOMEGALY		HB@	TC	DC			PLATELETS	HRP2/PLDH		PERIPHERAL SMEAR		Final Daignosis
				FEVER	CHILLS & RIGORS	SWEATING	HEADACHE	PAIN ABDOMEN	ALTERED SENSORIUM	OTHERS		PALLOR	ICTERUS	PETECHIAE OR PURPURA		SIZE IN CMS	CONSISTENCY	SIZE IN CMS	CONSISTENCY			N%	L%	M%		PI.V	PI.F	Thick	Thin	
108	1454564	11	M	P	A	A	A	A	A	A	95.4		A	A	S	1	Soft	3	soft	9.3	9100	62	32	6	1.5	-	-	-	-	Viral Fever
109	11454695	9	F	P	P	A	A	A	A	VO	76.2		A	A	S	A	-	3	soft	10.2	4500	62	32	6	1.09	+	-	-	PV	vivax.mal
110	1454365	12	M	P	A	A	A	A	A	A	85.4		A	A	S	A	-	A	-	10	7000	56	42	2	3.3	-	-	-	-	Viral Fever
111	507397	9	F	P	P	A	A	A	A	A	86.3		A	A	S	2	Soft	2	soft	8.2	7800	46	50	4	2.6	+	-	-	PV	vivax.mal
112	507359	7	F	P	A	A	A	A	A	A	81.8		A	A	S	2.5	Soft	A	-	8.4	9200	56	42	2	3.3	-	-	-	-	Viral Fever
113	1454753	10	F	P	A	A	A	P	A	A	76.2		A	A	S	A	-	A	-	9.5	7000	56	42	2	3.3	-	-	-	-	Viral Fever
114	1454738	11	M	P	A	A	A	A	A	A	85.2		A	A	S	1.5	Soft	A	-	8.6	8300	73	20	7	2.2	-	-	-	-	Viral Fever
115	1438380	7	M	P	A	P	A	A	A	A	77.2		A	A	S	1	Soft	3	firm	9.9	7400	62	32	6	1.5	-	-	-	-	Enteric Fever
116	1454762	8	F	P	A	A	P	A	A	A	74.5		A	A	S	2	Soft	A	-	10	6500	58	40	2	2.2	-	-	-	-	Viral Fever
117	1454773	6	M	P	A	A	A	A	A	A	80.2		A	A	S	A	-	3.5	soft	7	7000	56	42	2	3.3	-	-	-	-	Viral Fever
118	1454537	12	F	P	P	A	A	A	A	A	81.2		A	A	S	2	Soft	2	soft	9.8	7400	64	34	2	3.1	-	-	-	-	Viral Fever
119	507402	12	F	P	A	A	P	A	A	A	85.4		A	A	S	1.5	Soft	3.5	soft	9	27000	60	37	3	1.54	+	-	-	PV	vivax.mal
120	1457083	10	M	P	P	A	A	A	A	A	86.2		A	A	S	A	-	1.5	soft	10.4	8400	70	28	2	1.5	-	-	-	-	Viral Fever
121	1455768	11	M	P	A	A	A	P	A	A	86.4		A	A	S	2	Soft	2	soft	8	4500	46	50	4	1.02	+	-	-	PV	vivax.mal
122	145642	9	F	P	A	A	A	A	A	A	86.3		A	A	S	A	-	3	soft	11.3	7000	56	42	2	3.3	-	-	-	-	Enteric Fever
123	1455425	8	F	P	P	A	A	A	A	VO	76.2		A	A	S	2.5	Soft	A	-	12	6200	78	22	0	0.46	+	-	-	PV	vivax.mal
124	1455115	12	F	P	A	A	A	A	A	A	86.2		A	A	S	2.5	Soft	3	soft	7	9100	62	32	6	1.5	-	-	-	-	Viral Fever
125	1483063	4	M	P	A	A	P	A	A	A	88.6		A	A	S	1.5	Soft	1	soft	10	11200	58	40	2	1.45	+	-	-	PV	vivax.mal
126	145001	12	M	P	A	A	A	A	A	A	75.6		A	A	S	A	-	A	-	12	7000	56	42	2	3.3	-	-	-	-	Viral Fever
127	1454867	8	F	P	A	A	A	A	A	A	74.5		A	A	S	3	Soft	2	soft	11.3	3300	43	51	6	1.5	-	-	-	-	Viral Fever
128	1454817	9	M	P	A	A	A	P	A	A	86.3		A	A	S	1.5	Soft	2.5	soft	9.8	8600	44	48	3	2.4	-	+	PL.F	PL.F	Fal Malaria
129	1458337	12	F	P	A	A	A	A	A	A	84.2		A	A	S	2	Soft	2	firm	8.5	11900	70	28	2	1.5	-	-	-	-	Enteric Fever
130	1453996	9	M	P	A	A	A	P	A	A	86.3		A	A	S	1.5	Soft	A	-	8	12500	55	39	6	1.4	+	-	-	PV	vivax.mal
131	1483830	6	M	P	A	A	A	A	A	VO	80.4		A	A	S	A	-	2	soft	12	4500	30	68	2	1.2	+	-	-	PV	vivax.mal
132	145577	7	F	P	P	P	A	A	A	A	90.9		A	A	S	2	Soft	1	soft	13	8600	62	32	6	1.5	-	-	-	-	Viral Fever
133	145650	10	M	P	A	A	A	P	A	A	76.2		A	A	S	A	-	3	firm	10.2	7000	56	42	2	3.3	-	-	-	-	Enteric Fever
134	1455424	9	M	P	A	A	A	A	A	A	86.36		A	A	S	1.5	Soft	3	soft	9.4	6700	64	34	2	3.1	-	-	-	-	Viral Fever
135	145010	10	F	P	P	A	A	A	A	VO	76.4		A	A	S	1	Soft	3	soft	9.4	10000	60	36	4	1.14	+	-	-	PV	vivax.mal
136	1454853	6	M	P	A	A	A	P	A	A	80.2		A	A	S	2	Soft	A	-	8.5	8300	73	20	7	2.2	-	-	-	-	Viral Fever
137	1454547	5	M	P	A	A	A	A	A	A	94.5		A	A	S	1	Soft	3	soft	9.1	9400	42	57	7	1.2	+	-	-	PV	vivax.mal
138	1453106	10	F	P	A	A	P	A	A	A	76.2		A	A	S	2	Soft	2.5	soft	8.7	7500	62	32	6	1.5	-	-	-	-	Viral Fever
139	1483839	12	F	P	A	A	A	P	A	A	84.2		A	A	S	1	Soft	1.5	soft	10	9400	46	47	6	1.2	+	-	-	PV	vivax.mal
140	1483849	8	M	P	P	A	A	A	A	A	78.2		A	A	S	3	Soft	2.5	firm	10.5	7000	56	42	2	3.3	-	-	-	-	Enteric Fever
141	1455167	7	F	P	A	A	A	A	A	A	90.9		A	A	S	2	Soft	1	soft	12	6300	58	40	2	2.2	-	-	-	-	Viral Fever
142	145640	10	M	P	A	P	A	A	A	A	84.2		A	A	S	3	Soft	1	soft	8.7	5300	70	28	2	1.5	-	-	-	-	Viral Fever
143	1455424	11	F	P	A	A	A	A	A	VO	95.7		A	A	S	1	Soft	2	soft	12	7000	56	42	2	3.3	+	-	-	PV	vivax.mal
144	1455414	9	M	P	A	A	A	A	A	A	86.3		A	A	S	1.5	Soft	A	-	9	4300	62	32	6	1.5	+	-	-	-	Viral Fever
145	1455062	6	M	P	P	A	A	A	A	A	80.4		A	A	S	A	-	3	soft	10.2	1800	58	40	2	1.39	+	-	-	PV	vivax.mal
146	145000	12	F	P	A	A	A	A	A	A	75.9		A	A	S	3	Soft	A	-	10	9400	64	34	2	3.1	-	-	-	-	Viral Fever
147	1454866	11	M	P	A	A	P	A	A	A	95.7		A	A	S	1	Soft	2.5	soft	11	8500	70	28	2	1.5	-	-	-	-	Enteric Fever
148	1454843	10	M	P	A	A	A	A	A	A	85.6		A	A	S	2	Soft	3	soft	9	7000	56	42	2	3.3	-	-	-	-	Viral Fever
149	1454737	8	M	P	A	A	P	A	A	VO	78.6		A	A	S	A	-	1	soft	6.5	11800	46	47	6	0.45	+	-	-	PV	vivax.mal
150	1454537	7	F	P	A	A	A	A	A	A	90.6		A	A	S	2.5	Soft	1	soft	12	7400	62	32	6	1.5	-	-	-	-	Viral Malaria
151	1454366	10	F	P	A	A	A	A	A	A	84.2		A	A	S	2	Soft	A	-	13	6400	43	51	6	1.5	-	-	-	-	Enteric Fever
152	1454996	9	F	P	A	A	A	A	A	A	86.4		A	A	S	1	Soft	2.5	soft	10.5	7000	56	42	2	3.3	-	-	-	-	Viral Fever
153	1483819	6	M	P	P	P	P	A	A	A	87.5		A	A	S	2.5	Soft	2	soft	10	5400	58	40	2	2.2	-	-	-	-	Viral Fever
154	1453840	12	F	P	A	A	A	P	A	A	86.4		A	A	S	A	-	A	-	11.5	10200	45	50	5	0.3	-	+	PL.F	PL.F	Fal Malaria
155	145021	11	M	P	A	A	A	A	A	A	95.2		A	A	S	2	Soft	1.5	soft	12	4400	64	34	2	3.1	-	-	-	-	Viral Fever
156	1454863	12	M	P	A	A	A	A	A	A	91.2		A	A	S	3	Soft	2	soft	10.1	8765	70	28	2	1.5	-	-	-	-	Viral Fever
157	1454176	10	F	P	A	A	A	A	A	A	86.5		A	A	S	2	Soft	A	-	9.4	7000	56	42	2	3.3	-	-	-	-	Viral Fever
158	1083848	9	M	P	P	A	A	A	A	A	78.5		A	A	S	1.5	Soft	A	-	8.7	6654	62	32	6	1.5	-	-	-	-	Viral Malaria
159	1458369	8	M	P	A	A	P	P	A	A	95.4		A	A	S	2	Soft	1	soft	9	6200	68	60	2	2.5	+	-	-	PV	vivax.mal
160	1458346	11	M	P	A	A	A	A	A	A	73.2		A	A	S	A	-	1	soft	8	7000	56	42	2	3.3	-	-	-	-	Viral Fever